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## Does endometriosis affect professional life? – a retrospective matched case-control study

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# Does endometriosis affect professional life? – a retrospective matched case-control study

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1  
2  
3 35 **Abstract**  
4

5 36 **Objectives:** Endometriosis is a gynaecologic disease causing severe and chronic  
6  
7  
8 37 pelvic pain as well as an impaired quality of life. The aim of this study was to  
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11 38 investigate if and how endometriosis interferes with professional choices, career  
12  
13 39 development and daily working life.

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15  
16 40 **Design, setting and participants:** Within a multicentre retrospective case-control  
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18  
19 41 study, we collected data from 505 women with surgically/ histologically confirmed  
20  
21 42 diagnosis of endometriosis and 505 matched controls. Study participants were  
22  
23 43 recruited in hospitals and private practices in Switzerland, Germany and Austria. The  
24  
25 44 study investigated work life and career paths of participants using a detailed  
26  
27 45 questionnaire.

28  
29  
30 46 **Main outcome measures:** Quantitative and qualitative parameters of professional  
31  
32 47 life as well as associations between endometriosis related symptoms and loss of  
33  
34 48 working power.

35  
36  
37 49 **Results:** Among women with endometriosis, chronic pain significantly increased sick  
38  
39 50 leave (OR = 3.52, 95%-CI: 2.02 - 6.13,  $R^2 = 0.072$ ,  $p < 0.001$ ). Higher frequency of  
40  
41 51 fatigue likewise related to increased sick leave (OR = 3.50, 95%-CI = 1.76 - 6.94,  $R^2$   
42  
43 = 0.073,  $p < 0.001$ ). Women with endometriosis had to consider health related  
44  
45 52 aspects in their career decisions to a significantly higher degree than women from  
46  
47 53 the control group (OR = 3.08, 95%-CI: 2.14 - 4.42,  $R^2 = 0.062$ ,  $p < 0.001$ ). However,  
48  
49 54 most other direct associations between endometriosis and work outcomes were very  
50  
51 55 weak (i.e.,  $R^2 < 0.03$ ). Notably, women with endometriosis did not experience higher  
52  
53 56 stress levels at work than controls when adjusted for confounders (OR = 1.17, 95%-  
54  
55 57 CI: 0.91 - 1.50,  $R^2 = 0.014$ ,  $p = 0.211$ ).  
56  
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3 59 **Conclusions:** Endometriosis has a negative impact on professional life. Disease  
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5  
6 60 symptoms result in health-related limitations of career choices. Further research to  
7  
8 61 develop strategies to support endometriosis affected women in realizing professional  
9  
10 62 opportunities is recommended.  
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13 63

#### 14 64 **Strength and limitations of this study**

15  
16  
17 65 This study presents one of the largest samples investigating the association between  
18  
19 66 endometriosis and professional activity.

20  
21 67 Recruitment of study participants in university, in district hospitals and in private  
22  
23 68 offices supports a representative sample.

24  
25 69 Validation of diagnosis and stage of endometriosis by operation reports provides high  
26  
27 70 data quality.

28  
29  
30 71 A combination of objective data and the personal experience of women diagnosed  
31  
32 72 with endometriosis provides valuable insight in professional activity on the  
33  
34 73 background of the disease.

35  
36 74 Given the retrospective design with a self-reported questionnaire, distortions in the  
37  
38 75 sense of falsely or overly attributing professional dissatisfaction to endometriosis  
39  
40 76 cannot be excluded.  
41  
42  
43 77

#### 44 45 78 **Trial registration number:**

46  
47 79 Clin.trial.gov: Endo\_QOL NCT02511626  
48  
49 80

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54  
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3 844  
5 **85 Conflict of interest**6  
7 86 The authors do not have any conflicts of interest.  
8

9 87

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11 **88 Data sharing statement**12  
13 89 The data set is available on request from the corresponding author.  
14  
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16 90

17  
18 **91 Key words:** Endometriosis, work, professional life, stress, career choice  
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24 **94 Introduction**25  
26  
27 9528  
29 96 Endometriosis is a gynaecologic disease, which is defined by the presence of  
3031 97 endometrium-like tissue outside the uterine cavity.[1] The prevalence of the disease  
3233 98 among women of reproductive age is estimated to be between 8 and 10%.[2,3]  
3435 99 Women suffering from endometriosis most commonly experience one or a multitude  
3637  
38 100 of the following symptoms: chronic pelvic pain, severe dysmenorrhea, deep  
3940 101 dyspareunia, pain during defecation/ urination, loin pain, irregular bleeding,  
4142 102 constipation/ diarrhoea, but also reduced fertility and chronic fatigue.[4,5] Numerous  
4344 103 and severe symptoms, the chronicity of the disease, side-effects of therapies as well  
4546 104 as the diagnostic delay[6,7] significantly affect women's global quality of life including  
4748 105 professional performance and place high demands on the treating physicians.[8,9,10]  
4950 106 For most patients, available treatment options, such as analgesics, different  
5152 107 hormonal therapies, and radical laparoscopy[1] are often not curative and associated  
5354 108 with significant side effects.[8,11]  
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2  
3 109 Consequently, disease symptoms, especially endometriosis-associated pain and  
4  
5 110 fatigue, may disturb the development and realization of long-term goals such as a  
6  
7 111 professional career[12] as well as meeting demands on the job. About 40% of  
8  
9 112 women with endometriosis report an impaired career growth through  
10  
11 113 endometriosis[9], and about 50% experience decreased work ability due to their  
12  
13 114 chronic disease.[8,13]

15 115 The quality of working life is a major aspect in overall quality of life,[14] which in turn  
16  
17 116 is the most important predictor of total cost of disease.[15] About 66% to 75% of total  
18  
19 117 costs of endometriosis arise from loss of working power and not from direct costs of  
20  
21 118 treatment.[15,16] Being able to work in a desired occupation may not only have a  
22  
23 119 strong impact on the personal financial situation and on the perception of daily work,  
24  
25 120 but can also be an important health factor. For example, unsatisfactory work  
26  
27 121 situations and poor possibilities for change are associated with increased levels of  
28  
29 122 headache, fatigue and depressed mood.[17]

32 123 High amounts of sick leave and impaired work productivity can put affected women  
33  
34 124 under observation and pressure to deliver full performance.[18,19] The rather  
35  
36 125 intimate and gender specific nature of the most common endometriosis symptoms,  
37  
38 126 tends to make affected women feel embarrassed. Consequently, they avoid to  
39  
40 127 discuss these problems with superiors and colleagues, particularly if these are  
41  
42 128 male.[20,21] Due to the invisibility of their disease, they can easily be perceived as  
43  
44 129 malingerers.[20] Therefore, medical professionals need to know about possible  
45  
46 130 difficulties endometriosis can bring on daily working life and professional  
47  
48 131 development; notably as endometriosis affected women repeatedly emphasize their  
49  
50 132 wish for a joint management and guidance from medical professionals, instead of  
51  
52 133 isolated treatment of endometriosis symptoms.[20,22,23] However, research on  
53  
54 134 quantitative and qualitative impairment of working life as the necessary background

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3 135 for adequate counselling is scarce and relies mainly on interview studies with rather  
4  
5 136 small samples of affected women.[19,20]

6  
7 137 Therefore, it was the aim of the present study to investigate (i) career development,  
8  
9 138 (ii) current work performance and (iii) the association between specific disease  
10  
11 139 symptoms and work performance in women diagnosed with endometriosis compared  
12  
13 140 to control women.

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## 17 18 142 **Material and Methods**

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21 143

### 22 23 144 **Study design**

24  
25 145 The study is designed as a multicentre retrospective case-control study. Main  
26  
27 146 outcome measures are the health limitations in career choice and the perceived  
28  
29 147 impact of endometriosis on current work life. Secondary outcome measures  
30  
31 148 investigate the gradual impact of endometriosis on the professional life in association  
32  
33 149 to endometriosis characteristics as well as endometriosis-associated symptoms.

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35  
36 150 The study has been conducted and reported applying the criteria of the STROBE  
37  
38 151 Statement.[24]

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### 42 43 153 **Recruitment**

44  
45 154 Recruitment of study participants is shown in Figure I. Study participants were  
46  
47 155 recruited between January 2010 and December 2015 at the following hospitals and  
48  
49 156 associated private practices in Switzerland, Germany and Austria: the University  
50  
51 157 Hospital Zurich, the Triemli Hospital Zurich, the district hospitals in Schaffhausen,  
52  
53 158 Solothurn, St. Gallen, Winterthur, Baden and Walenstadt, the Charité Berlin, the  
54  
55 159 Vivantes Humboldt Hospital Berlin, the Albertinen Hospital Hamburg, the University



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2  
3 160 Hospital Aachen and the University Hospital Graz. A smaller proportion of the study  
4  
5 161 population (N = 74, 66 of which could be included in the final analysis (13.1% of total  
6  
7 162 case group)) was recruited through different self-help groups for endometriosis  
8  
9 163 patients in Germany. Education level and family income are similar in this cohort and  
10  
11 164 the main group. However, this cohort was significantly older than the hospital group  
12  
13 165 ( $42.45 \pm 6.03$  versus  $37.02 \pm 7.21$  years,  $p < 0.001$ ), showed a longer time since  
14  
15 166 primary diagnosis ( $82.11 \pm 8.36$  versus  $37.20 \pm 44.00$  months,  $p < 0.001$ ) and  
16  
17 167 presented a significantly higher current stage of disease ( $p = 0.013$ ).

18  
19  
20 168 The recruitment of study participants was carried out via direct approach of health  
21  
22 169 care professionals. The questionnaire was explained to the respondent and  
23  
24 170 information about the voluntary nature of participation as well as anonymity of reports  
25  
26 171 and publications of its data was provided. Each participant received a detailed written  
27  
28 172 description of the study and signed informed consent. Participants were given all  
29  
30 173 documents and a return envelope. Control women were recruited either during  
31  
32 174 regular annual gynaecological consultation or stationary hospital stays because of  
33  
34 175 benign gynaecological problems other than endometriosis, and were matched to the  
35  
36 176 patient cohort in respect to age and ethnical background (pair-matching). Each  
37  
38 177 woman diagnosed with endometriosis was matched to a control woman recruited in  
39  
40 178 the same centre for age ( $\pm 3$  years) and ethnic background.

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43  
44 179 Inclusion criteria: All study participants had to be between 18 and 50 years. Women  
45  
46 180 diagnosed with endometriosis were included irrespective of disease symptoms but  
47  
48 181 only in case of surgically and histologically confirmed diagnosis. Only data sets with  
49  
50 182 at least 80% of answers for main and secondary outcome measures were included.

51  
52 183 Exclusion criteria: Women were excluded in case of current pregnancy and linguistic,  
53  
54 184 mental or psychological impairment that might affect understanding and completing  
55  
56 185 of the questionnaire.

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3 186 The most frequent reasons reported for not participating were lack of time and the  
4  
5 187 intimate nature of some of the questions. To maximize the return rate women were  
6  
7 188 reminded to complete and return the questionnaire after one and three months.  
8

9 189

## 10 11 190 **Questionnaire**

12  
13 191 The structured self-administered questionnaire contains 390 questions for all  
14  
15 192 participants and 90 additional specific questions for women diagnosed with  
16  
17 193 endometriosis.

18  
19  
20 194 It was developed on the background of current literature and clinical experience by  
21  
22 195 specialists for endometriosis of the University Hospital of Zurich and the central  
23  
24 196 board from the endometriosis self-help groups in Germany. The questionnaire  
25  
26 197 focuses on different aspects of quality of life as well as on factors possibly influencing  
27  
28 198 the development of endometriosis. It covers personal demographic data, life style  
29  
30 199 factors, a full gynaecological history and detailed information about the development,  
31  
32 200 symptoms and treatment of endometriosis. Questions about chronic pain concern  
33  
34 201 frequency, duration and intensity and were part of a modified form of the Brief Pain  
35  
36 202 Inventory[25] and the Pain Disability Index[26,27]. Different internationally validated  
37  
38 203 questionnaires investigate aspects of quality of life such as general well-being,  
39  
40 204 sexuality, partnership, and professional life.  
41  
42  
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45  
46 206 The current analysis focused on 26 questions about professional life: A first question  
47  
48 207 addressed highest achieved education level with six preselected answers (lower  
49  
50 208 school education, higher school education, apprenticeship, university degree, no  
51  
52 209 formal education, other). Women had to report the level of their current employment  
53  
54 210 (five preselected answers: full time, part time, full time housekeeping, in education,  
55  
56 211 registered as unemployed), their current own monthly net income (six preselected

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3 212 answers ranging from none to > 2500 Euros/ > 6000 Swiss francs respectively), their  
4  
5 213 family income and whether they currently worked in their job of choice (yes/ no), how  
6  
7 214 they perceived the level of their qualification for the currently held job (three  
8  
9 215 preselected answers: overqualified, about right, underqualified), the length of their  
10  
11 216 professional experience (< 5 years, 5 - 10 years and > 10 years), their years working  
12  
13 217 with the current employer (< 1 year, 1 - 5 years, 5 - 10 years, > 10 years), and the  
14  
15 218 subjectively perceived influence of health limitations on career choice (not at all, little,  
16  
17 219 medium, strongly, most important factor), as well as the perceived current level of  
18  
19 220 stress on the job (scale from 0 = none to 10 = very strong).

21  
22 221 Additional questions focussed on potential consequences of endometriosis on work  
23  
24 222 performance and sick-leave, e.g. missed working time, days worked despite  
25  
26 223 endometriosis symptoms per year, loss of productivity in relation to severity of  
27  
28 224 symptoms and reduction of work time and/ or giving up employment entirely due to  
29  
30 225 endometriosis. Answers to these questions relied on the women's perception of the  
31  
32 226 situation and were only asked to women diagnosed with endometriosis.

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### 36 37 228 **Verification of diagnosis and stage of endometriosis**

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39 229 To verify diagnosis, operation reports as well as the histological diagnosis of each  
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41 230 patient and each intervention were collected from medical charts. Stage was  
42  
43 231 classified according to the revised Classification of the American Society for  
44  
45 232 Reproductive Medicine (rASRM).[28]

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### 49 50 234 **Ethical approval**

51  
52 235 The study was approved by the Swiss ethics commission as well as by the ethic  
53  
54 236 boards of participating hospitals. This study followed the guidelines of the World  
55  
56 237 Medical Association Declaration of Helsinki 1964, updated in October 2013.

238

## 239 **Statistical analysis**

240 Differences in sample characteristics between study groups were computed with  
241 either independent sample t-tests for continuous variables or Pearson  $\chi^2$ -tests for  
242 categorical variables. To test associations between study groups we conducted a  
243 series of either multinomial logistic regression for nominal-scaled outcomes or ordinal  
244 logistic regression for ordinal-scaled outcomes. The study group, that is, women with  
245 endometriosis versus controls without endometriosis, was always included as the  
246 independent predictor variable. The proportion of variance explained based on the  
247 study group was indicated by Nagelkerke's pseudo R<sup>2</sup>. Sample characteristics that  
248 differed significantly between study groups were statistically adjusted for by including  
249 them simultaneously as covariates. We applied Bonferroni correction to adjust the  
250 significance level  $\alpha$  for multiple testing. All analyses were conducted with SPSS  
251 version 24 for Windows.

252

## 253 **Results**

254

### 255 **Characteristics of study groups and possible confounders**

256 A comparison of socio-epidemiological parameters between women with  
257 endometriosis and control women is presented in Table I.

258 In the subgroups of women having at least one child (26.9% of the case group and  
259 47.1% of the control group) the proportional distribution of having a gainful  
260 occupation was as followed: 22.1% (N = 30) of endometriosis affected mothers  
261 worked full time versus 23.9% (N = 57) of control mothers, 50.0% (N = 68) of  
262 endometriosis affected mothers versus 57.1% (N = 136) of control mothers worked

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3 263 part time and 27.9% (N = 38) of endometriosis affected mothers versus 18.9% (N =  
4  
5 264 45) of control mothers did not follow any paid occupation.

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7 265 Disease characteristics of the endometriosis group are summarized in Table II.  
8  
9

10 266

### 11 12 13 267 **Parameters of working life**

14  
15 268 Characteristics of professional activity in women diagnosed with endometriosis and  
16  
17 269 control women are presented in Table III. In the unadjusted analyses, profession of  
18  
19 270 choice, health influences on career choice, adequacy of job qualification, professional  
20  
21 271 experience and stress on the job showed statistically significant differences in both  
22  
23 272 groups. However, except for health influences on career choice (R<sup>2</sup> = 0.062), the  
24  
25 273 proportion of variance explained by each factor was very small (all R<sup>2</sup> < 0.027). After  
26  
27 274 adjustment for confounders, the associations between a diagnosis of endometriosis  
28  
29 275 and reporting a lower likelihood of working in the job of choice (OR = 0.45), stronger  
30  
31 276 health influences on the selection of the professional activity (OR = 3.08), a higher  
32  
33 277 experience in the current profession (OR = 2.29) and a longer duration of the present  
34  
35 278 employment (OR = 1.65) remained statistically significant.  
36  
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38

39 279 The intensity of reported health related limitations in career choice was independent  
40  
41 280 of rASRM-stage ( $\chi^2$ , 16.51, df = 12, p = 0.169), but associated with the occurrence of  
42  
43 281 chronic pain (39.6% vs. 18.3%,  $\chi^2$ , 34.39, df = 4, p < 0.001) as well as with the  
44  
45 282 frequency of pain ( $\chi^2$ , 25.62, df = 8, p = 0.001).  
46  
47

48 283

### 49 284 **Work impairment and compensatory mechanisms**

50  
51  
52 285 Altogether, 87.6% of the women reported no sick leave due to endometriosis during  
53  
54 286 the month prior to the study period, 10,7% one to three days, 0,7% four to seven  
55  
56 287 days, 0,5% one to two 2 weeks, 0,5% two to four weeks of sick leave without bringing  
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3 288 any medical certificate to their employer. An additional 7,6% had to refrain from work  
4  
5 289 due to endometriosis between two and four weeks and collected a medical certificate  
6  
7 290 (most employers in Switzerland and Germany request a certificate only for more than  
8  
9 291 three days of absence). Asked for the last year, 60.2% of the women diagnosed with  
10  
11 292 endometriosis stated to have never submitted a medical certificate because of their  
12  
13 293 endometriosis. Instead, 13.1% of endometriosis patients used one week or more  
14  
15 294 over time or their vacation when they felt too sick to work. Furthermore, 75.5% of  
16  
17 295 women with endometriosis reported to have gone to work in spite of severe pain  
18  
19 296 during the previous month. A total of 89.2% women affirmed to have worked despite  
20  
21 297 pain in the year prior to the study. Out of these women, 89.8% remarked a loss of  
22  
23 298 work productivity, with 65.1% stating strong or very strong limitations. On days with  
24  
25 299 minimal endometriosis-symptoms still 75.3% felt some loss of productivity.  
26  
27  
28 300 A minority of women with endometriosis reported working part time (10.3%) or giving  
29  
30 301 up work entirely (5.8%) due to their disease (n = 445).  
31  
32

33 302

### 35 303 **Influence of endometriosis-associated symptoms on sick leave and** 36 37 304 **productivity loss**

39 305 We then examined whether different endometriosis symptoms were related to  
40  
41 306 absenteeism and impaired work productivity (Table IV). All four predictor variables  
42  
43 307 were significantly associated with sick leave during the most recent four weeks. The  
44  
45 308 occurrence of chronic pain as well as concomitant psychological symptoms were  
46  
47 309 associated with significantly higher degrees of perceived productivity loss, but effect  
48  
49 310 sizes were modest and accounted for less than 11% of variance explained.  
50

51 311

52 312

## 57 313 **Discussion**

314

315 Endometriosis, especially in association with chronic pain, interfered with  
316 professional activity: Women diagnosed with endometriosis showed a lower  
317 likelihood of working in their profession of choice and stronger health-related  
318 considerations on their career decisions. They had higher professional experience  
319 and had stayed longer in their current employment. Endometriosis-associated  
320 symptoms and symptom characteristics were moderately related to sick-leave and  
321 work impairment, but in contrast to our expectations, endometriosis was not  
322 associated with increased work-related stress levels in multivariate analysis.

323

324 Education level and salaries did not differ significantly between case and control  
325 group in our study (Table I); a result that has been described previously.[13] Other  
326 studies, however, reported serious effects of endometriosis on education, especially  
327 on tertiary formation,[8,20]. These contrasting findings might result from differences  
328 in study groups, for example with regard to the onset of disease symptoms in relation  
329 to education, professional training and professional activity. Many studies report an  
330 average age of first symptoms between 20 and 29 years,[6,29-31] i.e. an age in  
331 which most women have completed professional training. Other authors reported an  
332 earlier onset of disease symptoms,[32] and emphasize that endometriosis in  
333 adolescent girls is an underestimated problem.[31,33,34] An additional factor  
334 responsible for a different association between endometriosis and education vs.  
335 professional performance might be a higher tolerance for sick-leave and impaired  
336 energy levels in a school- or university setting compared to paid jobs.

337

338 According to the present results women with endometriosis were very successful in  
339 their health-related choice of future professions. Although health issues were

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2  
3 340 important criteria in the initial career choice and women diagnosed with  
4  
5 341 endometriosis do work less often in their desired profession, the resulting choice led  
6  
7 342 to a higher experience in the current profession as well as longer durations working  
8  
9 343 with the same employer (Table III). On one hand, women might prefer to stay with an  
10  
11 344 employer as soon as they found a professional environment adapted to their  
12  
13 345 endometriosis-related needs. On the other hand, they might fear to be unable to find  
14  
15 346 another job and consequently hesitate to change employment. However, our finding  
16  
17 347 that women with endometriosis do not experience higher levels of work-related stress  
18  
19 348 contradicts such assumptions. The fact that women with endometriosis had a lower  
20  
21 349 number of children than the control group may contribute to more stable long-term  
22  
23 350 employment as well as higher professional experience. The association between  
24  
25 351 children and professional activity is also reflected by a higher percentage of women  
26  
27 352 with a paid occupation in women with endometriosis compared to control women.  
28  
29 353 The assumption that the higher number of children of the control women led to more  
30  
31 354 interruptions and reductions of professional activity raises the question why we didn't  
32  
33 355 find higher qualification and consequently higher salaries in women diagnosed with  
34  
35 356 endometriosis. It is possible that professional impairments due to endometriosis and  
36  
37 357 reduction of professional activity due to motherhood balance each other out. This  
38  
39 358 hypothesis is supported by the finding that a very similar percentage of women  
40  
41 359 worked part time in both groups, although women diagnosed with endometriosis  
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43 360 more often remained childless. Comparing mothers with and without endometriosis,  
44  
45 361 those with endometriosis more often gave up work entirely. The triple challenge of  
46  
47 362 having children, dealing with a chronic disease like endometriosis and working in a  
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49 363 paid occupation might be too stressful for some of these women. Or – considering  
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51 364 infertility as a common symptom of endometriosis[4,5] – some women might make  
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3 365 motherhood a priority in their life after years of problems conceiving and quit work for  
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5 366 this reason.

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7 367 However, effect sizes in the direct associations between endometriosis and  
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9 368 professional activity were rather small. Altogether, these results show that except the  
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11 369 influence of health issues on professional decisions, differences between women  
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13 370 diagnosed with endometriosis and control women are minor and a successful long-  
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15 371 term professional activity can often be realized despite endometriosis.

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20 373 Although differences in professional activity between women diagnosed with  
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22 374 endometriosis and control women are small, productivity loss[9,15] as well as sick  
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24 375 leave[9,10] resulting from endometriosis are relevant issues for many women  
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26 376 diagnosed with endometriosis. Average loss of work time per week (absenteeism)  
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28 377 due to endometriosis is reported to be between 4.4 and 7.4 hours.[9,10]. In our study,  
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30 378 chronic pain, the frequency of pain, fatigue and psychological symptoms were  
31  
32 379 significantly - but with small effect sizes - related to higher amounts of sick leave  
33  
34 380 (Table IV). Productivity loss at work due to endometriosis-related symptoms was  
35  
36 381 described to be high or very high by up to 65% of women in the present study.  
37  
38 382 Struggles to fulfil normal demands of work might further be challenged by therapy  
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40 383 side effects, for example by dizziness from strong pain killers.[18,19] Using overtime  
41  
42 384 or vacation to compensate absences from work as well as saving energy for work  
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44 385 through reduction of leisure time activities seem to be part of the individual strategies  
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46 386 for successful work performance in women with endometriosis in our study and those  
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48 387 of others.[32]

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52 388 As for the relationship between rASRM stage and endometriosis-associated  
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54 389 symptoms,[1,3] none of the parameters evaluating professional activity showed any  
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56 390 significant association with rARSM stage. In contrast, most outcome measures were

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3 391 related to the occurrence and frequency of chronic pain, which is supported by other  
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5 392 studies on endometriosis[10,15] as well as on other chronic pain conditions such as  
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7 393 migraine or fibromyalgia.[35,36] Even if the effect size of pain in this study is small,  
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9 394 findings support the relevance of pain management for adequate work performance.  
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11 395 Exhaustion, either as a symptom of endometriosis or as a frequent comorbidity,[37]  
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13 396 interfered with professional activity in the present as well as in other studies.[1,9]

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18 398 Several authors reported elevated levels of general[38,39] as well as emotional[21]  
19  
20 399 distress in women diagnosed with endometriosis. Unfortunately, there are no  
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22 400 previous reports on work-specific stress in endometriosis affected women. With the  
23  
24 401 specific challenges of a high-quality work performance on the background of a  
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26 402 diagnosis of endometriosis, we expected these women to report higher levels of  
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28 403 work-related stress than control women. However, this expectation was not met even  
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30 404 though women reported to sometimes attend work despite endometriosis-associated  
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32 405 pain. As we investigated women whose initial diagnosis was up to 20 years ago, they  
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34 406 might meanwhile have found an occupation meeting their needs; and as a result of  
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36 407 the often long-term employment, superiors and colleagues might have adapted to  
37  
38 408 their sometimes reduced working ability. Also, the fact that work can be a source of  
39  
40 409 distraction and self-esteem for individuals suffering from a chronic disease,[40] may  
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42 410 offset stressful situations. Although the majority of women diagnosed with  
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44 411 endometriosis experienced no increased stress levels at work, 16.2% of the women  
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46 412 reduced or even gave up work entirely due to endometriosis-associated symptoms, a  
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48 413 development that has also been observed by others.[13] Such decisions may result  
49  
50 414 from feeling pressured to reduce or quit work when employers know about a chronic  
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52 415 disease as endometriosis.[8,20] More flexible work schedules, a generous policy  
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54 416 regarding sick-leave, sufficient breaks, adjusted physical demands, the possibility to

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3 417 lie down, and bathrooms nearby are estimated to be helpful resources for successful  
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5 418 professional performance in women with endometriosis.[19,20]

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9 420 This study presents one of the largest samples investigating the association between  
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11 421 endometriosis and professional life. Study participants were recruited in University, in  
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13 422 district hospitals and in private offices in order to collect a representative sample. The  
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15 423 pair matching with regard to age and ethnic background allowed to exclude these  
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17 424 factors as confounders. A meticulous revision of all operation reports by the same  
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19 425 investigator (AKS) ensured a high data quality with regard to diagnosis and  
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21 426 classification of endometriosis. The response rate of 64.1% in the case and 35.8% in  
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23 427 the control group is in the upper level of comparable studies.[8,9].

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26 428 Given the method of a self-reported questionnaire in a retrospective design,  
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28 429 distortions in the sense of falsely or overly attributing dissatisfaction on the job to  
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30 430 endometriosis cannot be excluded. However, such bias would result in  
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32 431 overestimation, but the associations found show rather limited effect sizes. By  
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34 432 addressing questions on professional activity either on the current situation or the  
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36 433 period just prior to study participation we tried to reduce recall bias.

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## 40 41 435 **Conclusion**

42  
43 436 Although endometriosis can have a severe impact on professional activity and  
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45 437 development, the majority of women experiences only small limitations of their work  
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47 438 performance when health issues are integrated into the choice of a future profession.  
48  
49 439 Disease symptoms as pains and fatigue may interfere with presence at work and the  
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51 440 quality of work performance, but most women succeed to integrate endometriosis-  
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53 441 associated needs without experiencing a higher degree of work-related stress.

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452 MLS: collection of data in Solothurn and Schaffhausen, interpretation of data, drafting  
453 and finalization of the manuscript

454 MPH: statistical analysis, interpretation of data, finalization of manuscript

455 AKS: investigator, collection of data at site Winterthur, Switzerland, verification of  
456 surgical reports, finalization of the manuscript

457 KG: concept of study, collection of data site Zurich, management databank,  
458 finalization of the manuscript

459 MR: investigator, collection of data at site Berlin, Germany, finalization of the  
460 manuscript

461 MW: investigator, collection of data at site Aachen, Germany, and Graz, Austria,  
462 finalization of the manuscript

463 FH: investigator, collection of data at site St. Gallen, Switzerland, finalization of the  
464 manuscript

465 SvO: investigator, collection of data at site Zurich, Switzerland, finalization of the  
466 manuscript

467 ME: investigator, collection of data at site Schaffhausen, Switzerland, finalization of  
468 the manuscript

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3 469 FM: concept of study, investigator at site Solothurn, Switzerland, finalization of  
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5 470 manuscript  
6  
7 471 BI: concept of study, investigator at site Zurich, Switzerland, interpretation of data,  
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9 472 finalization of manuscript  
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11 473 PI: concept of study, investigator and data collection at Zurich, Switzerland,  
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13 474 finalization of the manuscript  
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15 475 DF: concept of study, investigator at site Zurich, Switzerland, interpretation of data,  
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17 476 finalization of manuscript  
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19 477 BL: principal investigator, concept and conduct of study, investigator at site Zurich,  
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21 478 Switzerland, collection and analysis of data, preparation and finalization of  
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23 479 manuscript  
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595 **Tables**596 **Table I: Descriptive statistics and group comparisons**

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	P=0.344 <sup>a</sup>
Nationality	Swiss	N=211 (42.2%)	N=285 (57.3%)	P<0.001 <sup>b</sup>
	German	N=244 (48.8%)	N=161 (32.4%)	
	Others	N=45 (9.0%)	N=51 (10.3%)	
Marital status	Married/ Cohabiting	N=420 (83.3%)	N=397 (79.4.6%)	P=0.109 <sup>b</sup>
	Single	N=84 (16.7%)	N=103 (20.6%)	
Pregnancies >24 weeks	0	N=331 (70.6%)	N=245 (50.9%)	P<0.001 <sup>b</sup>
	1	N=83 (17.7%)	N=80 (16.6%)	
	≥2	N=55 (11.7%)	N=156 (32.4%)	
Education level <sup>c</sup>	Low	N=71 (14.4%)	N=74 (14.7%)	P=0.990 <sup>b</sup>
	Medium	N=245 (49.6%)	N=249 (49.4%)	
	High	N=178 (36.0%)	N=181 (35.9%)	
Paid occupation	Full-time	N=248 (49.8%)	N=206 (41.8%)	P=0.016 <sup>b</sup>
	Part-time	N=176 (35.3%)	N=186 (37.7%)	
	None	N=74 (14.9%)	N=101 (20.5%)	

597 <sup>a</sup>Independent samples t-test598 <sup>b</sup>Pearson  $\chi^2$ -test599 <sup>c</sup>Scale: Low="no formal education/ lower school education", Medium="higher school education/ apprenticeship",  
600 High="university degree"

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606 **Table II: Disease characteristics in women diagnosed with endometriosis**

<b>Criteria</b>	<b>Endometriosis Group N= 505</b>		
<b>Time since occurrence of first symptoms (N=474)</b>	less than 1 year	5.49%	26
	1 - 2 years	5.27%	25
	2 -5 years	28.06%	133
	6 -10 years	18.99%	90
	more than 10 years	42.19%	200
<b>rASRM-stage of endometriosis (N=502)</b>	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
<b>Number of endometriosis-related surgical interventions (N=505)</b>	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information	7.33%	37
	Mean ± SD	1.79 ± 1.27	

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614 **Table III: Associations between endometriosis and characteristics of pro-**  
 615 **fessional activity including the proportion of variance explained by the disease**

Outcome	Reference category	Unadjusted OR (95% CI)	Adjusted OR** (95% CI)	R <sup>2</sup>
Own income	1 point increase <sup>a</sup>	1.26 (0.99; 1.60)	1.09 (0.81; 1.47)	0.004
Profession of choice	Yes	0.47 (0.34; 0.65)*	0.45 (0.31; 0.66)*	0.026
	Partially	0.67 (0.45; 1.00) Ref.	0.65 (0.42; 1.02)	
	No			
Degree of health influences on career choice	1 point increase <sup>b</sup>	2.92 (2.10; 4.04)*	3.08 (2.14; 4.42)*	0.062
Estimation of adequacy of job qualification	too high	1.82 (1.18; 2.80)*	1.47 (0.92; 2.36)	0.011
	too low	1.25 (0.89; 1.77)	1.21 (0.83; 1.77)	
	adequate	Ref.		
Professional experience	1 point increase <sup>c</sup>	1.63 (1.28; 2.07)*	2.29 (1.73; 3.03)*	0.019
Duration of current employment	1 point increase <sup>d</sup>	1.36 (1.07; 1.74)	1.65 (1.26; 2.16)*	0.008
Work-related stress level	1 point increase <sup>e</sup>	1.50 (1.20; 1.89)*	1.17 (0.91; 1.50)	0.014

616 \* Statistically significant at Bonferroni corrected  $\alpha = 0.007$

617 \*\* Adjusted for nationality, number of pregnancies, and occupation

618 <sup>a</sup> Scale: 1= $\leq$ 3000 CHF (1000 EUR), 2=3001-6000 CHF (1001-3000 EUR), 3= $\geq$ 6000 CHF (>3000 EUR) per month

619 <sup>b</sup> Scale: 1="not at all", 2="moderately", 3="strongly"

620 <sup>c</sup> Scale: 1= $<$ 5 years, 2=5-10 years, 3= $\geq$ 10 years

621 <sup>d</sup> Scale: 1= $<$ 1 year, 2=1-5 years, 3=5-10 years, 4= $\geq$ 10 years

622 <sup>e</sup> Scale: 0="no stress at all" – 10="extreme stress"

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626 **Table IV: Association of endometriosis-related symptoms to sick leave and**  
 627 **productivity loss in the last four weeks**

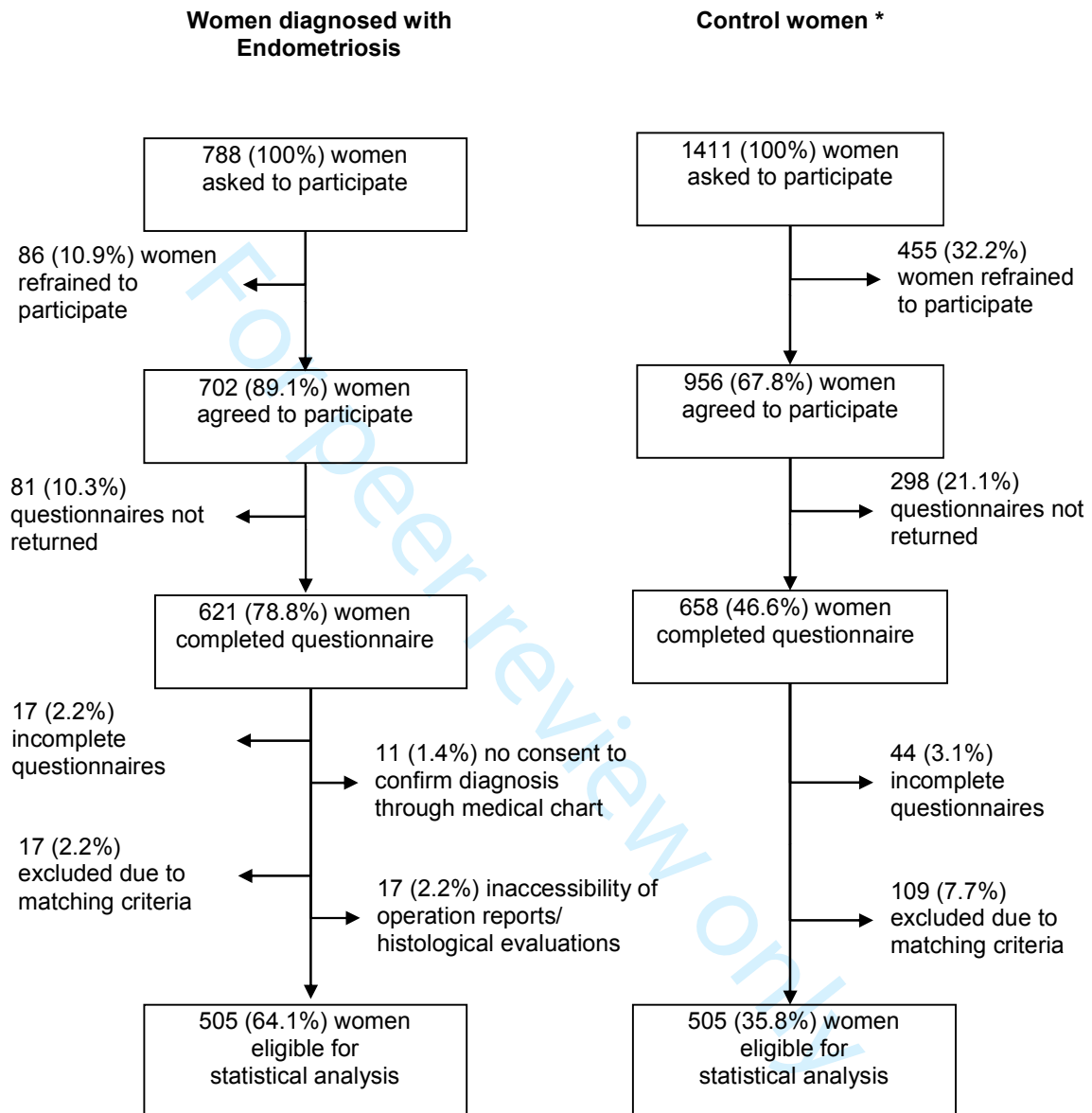
Predictor		Sick leave <sup>a</sup>		Productivity loss <sup>b</sup>	
		OR (95% CI)	R <sup>2</sup>	OR (95% CI)	R <sup>2</sup>
Chronic pain	Yes	3.52 (2.02;	0.072	3.08 (2.11; 4.50)*	0.087
	No	6.13)*Ref.			
Frequency of pain	Daily	2.82 (1.47;	0.053	1.81 (1.05; 3.12)	0.040
	>1 per week	5.39)*			
	≤1 per week	1.40 (0.66; 2.97) Ref.			
Frequency of fatigue	Frequently	3.50 (1.76;	0.073	3.99 (2.49; 6.39)	0.107
	Sometimes	6.94)*			
	Rarely	1.15 (0.50; 2.64) Ref.			
Psychological symptoms	Yes	3.03 (1.77;	0.061	2.90 (1.98; 4.23)*	0.082
	No	5.18)* Ref.			

628 \* Statistically significant at Bonferroni corrected  $\alpha=0.01$

629 <sup>a</sup> Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days

630 <sup>b</sup> Refers to current maximal impairments; Scale: 1="not at all/ little", 2="moderately/ strong", 3="very strong"

**Flow chart I. Recruitment of study participants**



\* women presenting for routine gynaecological care or benign gynaecological surgery

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8/9
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	7

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).



# BMJ Open

## Does endometriosis affect professional life? – a matched case-control study

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<b>Primary Subject Heading</b>:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

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Manuscripts

# 1 Does endometriosis affect professional life? – 2 a matched case-control study

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21 Switzerland

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23  
24  
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27  
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1  
2  
3 35 **Abstract**  
4

5 36 **Objectives:** Endometriosis is a gynaecological disease most commonly causing  
6  
7  
8 37 severe and chronic pelvic pain as well as an impaired quality of life. The aim of this  
9  
10  
11 38 study was to investigate if and how endometriosis affects choices regarding  
12  
13 39 professional life as well as the quality of daily working life.  
14  
15

16 40 **Design, setting, and participants:** In the context of a multicentre case-control  
17  
18  
19 41 study, we collected data from 505 women with surgically/histologically confirmed  
20  
21 42 diagnosis of endometriosis and 505 matched controls. Study participants were  
22  
23 43 recruited prospectively in hospitals and doctors' practices in Switzerland, Germany,  
24  
25 44 and Austria. Using a detailed questionnaire, the study investigated work-life and  
26  
27 45 career choices of study participants.  
28  
29

30 46 **Main outcome measures:** Quantitative and qualitative parameters of professional  
31  
32 47 life as well as associations between endometriosis related symptoms and a reduced  
33  
34 48 ability to work.  
35  
36

37 49 **Results:** Women with endometriosis were less often able to work in their desired  
38  
39  
40 50 profession than women from the control group (OR = 0.45, 95%-CI: 0.31 - 0.66,  $R^2$  =  
41  
42 51 0.026,  $p < 0.001$ ) and they had to take health-related limitations into consideration in  
43  
44 52 their career decisions to a significantly higher degree than women in the control  
45  
46 53 group (OR = 3.08, 95%-CI: 2.14 - 4.42,  $R^2$  = 0.062,  $p < 0.001$ ). Among women with  
47  
48 54 endometriosis, chronic pain was significantly associated with increased sick leave  
49  
50 55 (OR = 3.52, 95%-CI: 2.02 - 6.13,  $R^2$  = 0.072,  $p < 0.001$ ) as well as with loss of  
51  
52 56 productivity at work (OR = 3.08, 95%-CI: 2.11 - 4.50,  $R^2$  = 0.087,  $p < 0.001$ ).  
53  
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2  
3 57 **Conclusions:** Endometriosis is associated with impairment of professional life, in  
4  
5  
6 58 particular with regard to career choices. Further research to develop strategies to  
7  
8 59 support endometriosis-affected women in realizing professional opportunities is  
9  
10 60 recommended.

### 61 **Strengths and limitations of this study**

14 62 This study presents one of the largest samples investigating the association between  
15  
16 63 endometriosis and professional activity. It is one of the first studies in this field to  
17  
18 64 provide a matched control group.

21 65 Recruitment of study participants in university hospitals, in district hospitals and in  
22  
23 66 private doctors' practices ensured a representative sample.

25 67 Validation of diagnosis and stage of endometriosis by case reports provided high  
26  
27 68 data quality.

30 69 Given the design of the study (using a self-reported questionnaire answered  
31  
32 70 retrospectively), distortions in the sense of false or excessive attribution of  
33  
34 71 professional dissatisfaction to endometriosis cannot be excluded.

36 72 As we did not investigate diseases or symptoms that may also have had an impact  
37  
38 73 on professional life in the control group, results may be underestimated.

40  
41 74

### 43 75 **Trial registration number**

45 76 Clin.trial.gov: Endo\_QOL NCT02511626

47  
48 77

### 49 78 **Funding**

51 79 This research received no specific grant from any funding agency in the public,  
52  
53 80 commercial, or not-for-profit sectors.

55  
56 81

## 82 **Conflict of interest**

83 The authors do not have any conflicts of interest.

84

## 85 **Data sharing statement**

86 The data set is available on request from the corresponding author.

87

88 **Key words:** Endometriosis, work, professional life, stress, career choice

89

90

## 91 **Introduction**

92

93 Endometriosis is a gynaecological disease defined by the presence of endometrium-  
94 like tissue outside the uterine cavity.<sup>1</sup> The prevalence of the disease among women  
95 of reproductive age is estimated to be between 8 and 10%.<sup>2,3</sup>

96 Women suffering from endometriosis experience most commonly one or more of the  
97 following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia,  
98 pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea,  
99 as well as reduced fertility and chronic fatigue.<sup>4,5</sup> Numerous and severe symptoms,  
100 the chronicity of the disease, side effects of therapies as well as diagnostic delays<sup>6,7</sup>  
101 significantly affect women's overall quality of life, including professional performance,  
102 and place high demands on the treating physicians.<sup>8,9,10</sup> For most patients, available  
103 treatment options, such as analgesics, various hormonal therapies, and radical lapa-  
104 roscopy<sup>1</sup> are often not curative and are associated with significant side effects.<sup>8,11</sup>

105 Consequently, disease symptoms, especially endometriosis-related pain and fatigue,  
106 may disturb the development and realization of long-term goals such as a  
107 professional career<sup>12</sup> and may make it difficult to meet the demands of a job. About

1  
2  
3 108 40% of women with endometriosis report impaired career growth due to  
4  
5 109 endometriosis,<sup>9</sup> and about 50% experience a decreased ability to work due to their  
6  
7 110 chronic disease.<sup>8 13</sup> Differentiated knowledge on the nature of such limitations and in  
8  
9 111 particular on how adjustments to professional life can be made to improve  
10  
11 112 professional performance is currently lacking.

13 113 The quality of working life is a major aspect in quality of life overall,<sup>14</sup> which in turn is  
14  
15 114 the most important predictor of total cost of disease.<sup>15</sup> About 66% to 75% of the total  
16  
17 115 costs of endometriosis arise from reduced ability to work and not from direct costs of  
18  
19 116 treatment.<sup>15 16</sup> Being able to work in a desired occupation may not only have a strong  
20  
21 117 impact on a woman's financial situation and on the perception of and attitude toward  
22  
23 118 daily work, but can also be an important health factor. For example, unsatisfactory  
24  
25 119 work and limited possibilities for change are associated with increased levels of  
26  
27 120 headache, fatigue and depressed mood.<sup>17</sup>

28  
29  
30  
31 121 Frequent sick leave and reduced work productivity can put affected women under  
32  
33 122 observation by superiors and under greater pressure to deliver full performance.<sup>18 19</sup>

34  
35 123 The rather intimate and gender-specific nature of the most common endometriosis  
36  
37 124 symptoms tends to make affected women feel embarrassed.<sup>20</sup> Consequently, they  
38  
39 125 avoid discussing endometriosis-related problems with superiors and colleagues,  
40  
41 126 particularly if the superiors and colleagues are male.<sup>20 21</sup> Due to the invisibility of their  
42  
43 127 disease, they can be easily perceived as malingerers.<sup>20</sup> Therefore, medical  
44  
45 128 professionals need to know how the symptoms of endometriosis can affect daily  
46  
47 129 working life and professional development, notably because endometriosis-affected  
48  
49 130 women repeatedly underline their wish for comprehensive information<sup>20 22 23</sup> and  
50  
51 131 advice in managing their disease in daily life,<sup>22 23</sup> instead of isolated treatment of  
52  
53 132 endometriosis symptoms.<sup>20 22 23</sup> However, research on quantitative and qualitative  
54  
55 133 impairment of working life as the necessary background for offering adequate  
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2  
3 134 counselling is scarce and relies mainly on interview-based studies with small  
4  
5 135 samples of affected women<sup>19 20</sup>; there is only one other study that uses a control  
6  
7 136 group.<sup>10</sup> In addition, work-related stress in women diagnosed with endometriosis has  
8  
9 137 not been investigated yet.

10  
11 138 Therefore, it was the aim of the present study to investigate parameters of working  
12  
13 139 life of a larger number of endometriosis-affected women, and compare findings with  
14  
15 140 those of a matched control group. We investigated (i) perceived health-related  
16  
17 141 limitations in career decisions; (ii) quality of the current work situation; and (iii) the  
18  
19 142 association between endometriosis-related disease symptoms and work  
20  
21 143 performance.  
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27 144

## 27 145 **Material and Methods**

28  
29 146

### 30 147 **Study design**

31  
32 148 The study is designed as a multicentre case-control study. Main outcome measures  
33  
34 149 are health limitations in career choice as well as quality and stability of the current  
35  
36 150 work situation. Secondary outcome measures investigate the gradual impact of  
37  
38 151 different symptoms as well as localisation of endometriosis on sick leave and loss of  
39  
40 152 productivity. The study has been conducted and reported applying the criteria of the  
41  
42 153 STROBE Statement.<sup>24</sup>  
43  
44  
45  
46

47 154

### 48 155 **Recruitment**

49  
50 156 Recruitment of study participants is shown in Figure I. To detect a 10% difference  
51  
52 157 between cases and controls with an alpha of 0.05, a beta of 0.2 and a power of 0.8 a  
53  
54 158 sample size of 387 participants in each group is needed. With the inclusion of 505  
55  
56  
57  
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3 159 participants in both groups we consequently reached very high power, for example  
4  
5 160 99.1 for the detection of differences in desired profession or 99.7 for health-related  
6  
7 161 limitations in career choice. Study participants were recruited prospectively for a  
8  
9 162 research project on quality of life including professional activity in endometriosis-  
10  
11 163 affected women compared to control women. Study participants were recruited  
12  
13 164 prospectively for a research project on quality of life including professional activity in  
14  
15 165 endometriosis-affected women compared to control women. Recruitment took place  
16  
17 166 between January 2010 and December 2015 at the following hospitals and associated  
18  
19 167 doctors' offices in Switzerland, Germany and Austria: the University Hospital Zurich,  
20  
21 168 the Triemli Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St.  
22  
23 169 Gallen, Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes  
24  
25 170 Humboldt Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital  
26  
27 171 Aachen, and the University Hospital Graz. In doctors' offices one or several  
28  
29 172 gynecologists work together in a medical unit, district hospitals offer tertiary care  
30  
31 173 associated with a university (= institution with highest academic level).  
32  
33

34  
35 174 A smaller segment of the study population (N = 74, 66 of which could be included in  
36  
37 175 the final analysis (13.1% of total case group)) was recruited through different self-  
38  
39 176 help groups for endometriosis patients (in Germany only). Education levels and  
40  
41 177 family incomes in this cohort are similar to those in the main group. However, the  
42  
43 178 women in this cohort were significantly older than those in the hospital group ( $42.45 \pm$   
44  
45 179  $6.03$  versus  $37.02 \pm 7.21$  years,  $p < 0.001$ ), showed a longer time since primary  
46  
47 180 diagnosis ( $82.11 \pm 8.36$  versus  $37.20 \pm 44.00$  months,  $p < 0.001$ ), and presented at  
48  
49 181 the time of the study a significantly higher stage of disease ( $p = 0.013$ ).  
50  
51

52 182 The recruitment of study participants was carried out via direct approach by  
53  
54 183 healthcare professionals. The questionnaire was explained to the respondents and  
55  
56 184 information about the voluntary nature of participation as well as anonymity of data in  
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3 185 reports and publications was provided. Each participant received a detailed written  
4  
5 186 description of the study and signed informed consent. Participants were given all  
6  
7 187 documents and a return envelope. Control women were recruited during regular  
8  
9 188 annual or biennial gynaecological consultations, as part of standard healthcare in the  
10  
11 189 three countries where recruitment took place. In addition, women during hospital  
12  
13 190 stays because of temporary mild benign gynaecological problems other than  
14  
15 191 endometriosis were invited to participate in the study. Each control woman was  
16  
17 192 matched to a woman diagnosed with endometriosis for age ( $\pm$  3 years) and ethnic  
18  
19 193 background, ie Caucasian or not (pair matching).

20  
21  
22 194 Inclusion criteria: All study participants had to be between 18 and 50 years old.  
23  
24 195 Women with surgically and histologically diagnosed endometriosis were included  
25  
26 196 irrespective of stage, location of lesions, and severity and profile of symptoms. Only  
27  
28 197 data sets with at least 80% of answers for main and secondary outcome measures  
29  
30 198 were included.

31  
32  
33 199 Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic,  
34  
35 200 mental or psychological impairments that might affect their ability to understand and  
36  
37 201 to complete the questionnaire.

38  
39 202 The most frequent reasons reported for not participating were lack of time and the  
40  
41 203 intimate nature of some of the questions. To maximize the return rate, women were  
42  
43 204 reminded to complete and return the questionnaire after one month and after three  
44  
45 205 months.

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48 206

## 49 50 207 **Questionnaire**

51  
52 208 The structured self-administered questionnaire contained 390 questions for all  
53  
54 209 participants and 90 additional specific questions for women diagnosed with  
55  
56 210 endometriosis. It was developed on the basis of current literature and clinical

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2  
3 211 experience by endometriosis specialists of the University Hospital of Zurich and the  
4  
5 212 central boards of endometriosis self-help groups in Germany.

6  
7 213 All participants received questions regarding demographics; life style; general  
8  
9 214 wellbeing; general, gynaecological, and medical history; childhood experiences;  
10  
11 215 sexuality; partnership; and professional life. Women diagnosed with endometriosis  
12  
13 216 were additionally asked to provide detailed information on the diagnosis and  
14  
15 217 treatment of endometriosis, symptoms of endometriosis, sick leave, and productivity  
16  
17 218 loss due specifically to endometriosis.

18  
19  
20 219 The analysis was based on answers to the following questions: nationality (German,  
21  
22 220 Swiss, Austrian, other (with the possibility of entering nationality), age (years), marital  
23  
24 221 status (married/cohabiting/single), highest achieved education level (lower school  
25  
26 222 education, high school education, apprenticeship, university degree, no formal  
27  
28 223 education, other), current own monthly net income (six choices for responses ranging  
29  
30 224 from none to more than 2500 Euros/ none to more than 6000 Swiss francs,  
31  
32 225 respectively), numbers of pregnancies of more than 24 weeks of gestation. Women  
33  
34 226 had to report their levels of current employment (full-time/part-time/full-time  
35  
36 227 housekeeping/student/registered as unemployed) and whether they currently worked  
37  
38 228 in their desired profession (yes/no). This question does not ask about the current  
39  
40 229 place of employment but on the profession itself, eg for a woman who always wanted  
41  
42 230 to be a teacher, is she now able to work as a teacher? They were asked how they  
43  
44 231 perceived their level of qualification for the currently held job (overqualified, about  
45  
46 232 right, under-qualified), length of professional experience (< 5 years, 5 - 10 years, and  
47  
48 233 > 10 years), years working with the current employer (< 1 year, 1 - 5 years, 5 - 10  
49  
50 234 years, > 10 years), the subjectively perceived influence of health-related limitations  
51  
52 235 on career choice (not at all, little, medium, strongly, exclusively) and perceived  
53  
54 236 current level of stress on the job (scale from 0 = none to 10 = very strong).

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2  
3 237 The following questions were asked only to women diagnosed with endometriosis:  
4  
5 238 amount of time since first symptoms of endometriosis were noticed (less than 1 year  
6  
7 239 ago/1 year ago/2 - 5 years ago/6 - 10 years ago/more than 10 years ago), date of  
8  
9 240 first diagnosis of endometriosis (month and year), number of surgeries related to  
10  
11 241 endometriosis (1/2-3/4-6/7-10/>10), chronic pain (yes/no), duration of pain (< 1  
12  
13 242 year/1 - 3 years/4 - 5 years/6 - 10 years/11 - 20 years/> 20 years), frequency of pain  
14  
15 243 (a few times per year/a few times per month/several times per week/once a  
16  
17 244 day/several times a day/permanently), cyclic pain (yes/no), psychological symptoms  
18  
19 245 lasting more than three months estimated by the study participant to be related to  
20  
21 246 endometriosis, such as depressive mood/anxiety/reduced resilience (yes/no), days  
22  
23 247 worked despite pain during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4  
24  
25 248 weeks), frequency of fatigue or exhaustion due to endometriosis (never,  
26  
27 249 rarely/sometimes/often/very often), sick leave due to symptoms of endometriosis (not  
28  
29 250 specified) during the last month (never/1-3 days/4-7 days/1-2 weeks/2-4 weeks), sick  
30  
31 251 leave due to symptoms of endometriosis in the last year (never/1-7 days/1-2  
32  
33 252 weeks/2-4 weeks/4-8 weeks/8-12 weeks/> 12 weeks), estimated loss of productivity  
34  
35 253 due to endometriosis when symptoms are at their maximum or at their minimum  
36  
37 254 respectively (no loss/a little/somewhat/high), reduction of work time due to  
38  
39 255 endometriosis (no reduction/reduction of 25%/50%/75%), and giving up employment  
40  
41 256 entirely due to endometriosis (yes/no). (Chronic pelvic pain included dysmenorrhea  
42  
43 257 as well as non-menstrual pelvic pain.)  
44  
45  
46  
47

48 258 The study was registered at [clinicaltrials.gov](http://clinicaltrials.gov) (NCT 02511626), where further details  
49  
50 259 on the complete questionnaire are available.  
51

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53 260

54  
55 261 **Verification of diagnosis and stage of endometriosis**  
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3 262 To verify diagnosis and obtain information about localization of endometriosis  
4  
5 263 lesions, surgical records as well as the histological diagnosis of each patient and  
6  
7 264 each intervention were collected from medical charts. Stage was classified according  
8  
9 265 to the revised Classification of the American Society for Reproductive Medicine  
10  
11 266 (rASRM).<sup>25</sup>

12  
13 267

### 14 15 268 **Ethical approval**

16  
17 269 The study was approved by the Swiss ethics commission as well as by the ethics  
18  
19 270 boards of participating hospitals. This study followed the guidelines of the World  
20  
21 271 Medical Association Declaration of Helsinki 1964, updated in October 2013.

22  
23 272

### 24 25 273 **Statistical analysis**

26  
27 274 Differences in sample characteristics between study groups were computed with  
28  
29 275 either independent sample t-tests for continuous variables or Pearson  $\chi^2$ -tests for  
30  
31 276 categorical variables. To test associations between study groups and characteristics  
32  
33 277 of professional life, we conducted a series of either multinomial logistic regression for  
34  
35 278 nominal-scaled outcomes or ordinal logistic regression for ordinal-scaled outcomes.  
36  
37 279 The study group, ie women with endometriosis as opposed to controls without  
38  
39 280 endometriosis, was always included as the independent predictor variable. The  
40  
41 281 proportion of variance explained based on the study group was indicated by  
42  
43 282 Nagelkerke's pseudo R<sup>2</sup>. Sample characteristics that differed significantly between  
44  
45 283 study groups were statistically adjusted for by including them simultaneously as  
46  
47 284 covariates. Initially,  $\alpha$  was set at 5%. We applied Bonferroni correction to adjust the  
48  
49 285 significance level  $\alpha$  for multiple testing. All analyses were conducted with SPSS  
50  
51 286 version 24 for Windows.

52  
53 287

## 288 Results

289

### 290 Characteristics of study groups and possible confounders

291 A comparison of socio-epidemiological parameters between women with  
 292 endometriosis and control women is presented in Table I. Significant variables, eg  
 293 nationality, pregnancies, and paid employment, were included as covariates in  
 294 subsequent analyses on case-control effects.

295

296 **Table I: Descriptive statistics and group comparisons**

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	p=0.344 <sup>a</sup>
Nationality	Swiss	N=211 (42.2%)	N=285 (57.3%)	p<0.001 <sup>b</sup>
	German	N=244 (48.8%)	N=161 (32.4%)	
	Others	N=45 (9.0%)	N=51 (10.3%)	
Marital status	Married/ Cohabiting	N=420 (83.3%)	N=397 (79.4%)	p=0.109 <sup>b</sup>
	Single	N=84 (16.7%)	N=103 (20.6%)	
Pregnancies >24 weeks	0	N=331 (70.6%)	N=245 (50.9%)	p<0.001 <sup>b</sup>
	1	N=83 (17.7%)	N=80 (16.6%)	
	≥2	N=55 (11.7%)	N=156 (32.4%)	
Education level <sup>c</sup>	Low	N=71 (14.4%)	N=74 (14.7%)	p=0.990 <sup>b</sup>
	Medium	N=245 (49.6%)	N=249 (49.4%)	
	High	N=178 (36.0%)	N=181 (35.9%)	
Paid occupation	Full-time	N=248 (49.8%)	N=206 (41.8%)	p=0.016 <sup>b</sup>
	Part-time	N=176 (35.3%)	N=186 (37.7%)	
	None	N=74 (14.9%)	N=101 (20.5%)	
Occupation among mothers <sup>d</sup> only	Full-time	N= 30 (22.1%)	N= 57 (23.9%)	p=0.120 <sup>b</sup>
	Part-time	N= 68 (50.0%)	N= 136 (57.1%)	
	None	N= 38 (27.9%)	N= 45 (18.9%)	

297 <sup>a</sup>Independent samples t-test

298 <sup>b</sup>Pearson  $\chi^2$ -test

299 <sup>c</sup>Scale: Low="no formal education/ lower school education", Medium="higher school education/ apprenticeship"  
 300 High="university degree"

301 <sup>d</sup>women with at least one pregnancy >24 weeks

302

303 Disease characteristics of the endometriosis group are shown in Table II.

304 **Table II: Disease characteristics in women diagnosed with endometriosis**

Criteria	Endometriosis Group
----------	---------------------

		%	N
<b>Time since occurrence of first symptoms (N=474)</b>	< 1 year	5.49%	26
	1-2 years	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	> 10 years	42.19%	200
<b>rASRM-stage of endometriosis (N=502)</b>	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
<b>Number of endometriosis-related surgical interventions (N=505)</b>	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information	7.33%	37
	Mean $\pm$ SD	1.79 $\pm$ 1.27	
<b>Douglas obliteration (N=503)</b>	Yes	26.6%	134
	No	73.4%	369
<b>Involvement of sacrouterine ligaments (N=503)</b>	Yes	61.4%	309
	No	38.6%	194
<b>Involvement of Douglas (N=503)</b>	Yes	72.0%	362
	No	28.0%	141
<b>Intra-abdominal adhesions (N=504)</b>	Yes	74.8%	377
	No	25.2%	127
<b>Involvement of pelvic wall (N=503)</b>	Yes	74.8%	377
	No	25.2%	127
<b>Involvement of vaginal fornix or septum rectovaginal (N=503)</b>	Yes	12.7%	64
	No	87.3%	439
<b>Endometrioma (N=502)</b>	Yes	49.0%	246
	No	51.0%	256
<b>Chronic pain (N=500)</b>	Yes	58.40%	292
	No	41.60%	208
<b>Duration of chronic pain</b>	Less than 1 year	3.48%	10
	1 - < 3 years	13.59%	39
	3 - < 5 years	17.07%	49
	5 - < 10 years	23.34%	67
	10 - < 20 years	29.27%	84
	$\geq$ 20 years	13.24%	38
<b>Frequency of pain</b>	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
<b>Frequency of endometriosis-related fatigue/ exhaustion</b>	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Frequently	28.14%	141

	Very frequently	22.55%	113
<b>Psychological Symptoms due to endometriosis<sup>a</sup></b>	Yes	57.24%	261
	No	42.76%	195

<sup>a</sup>depressive mood/ anxiety/ reduced resilience of more than three months

### Parameters of working life

Parameters of professional activity in women diagnosed with endometriosis and control women are presented in Table IIIa.

**Table IIIa: Parameters of professional activity in the case and the control group**

Criteria	Endometriosis group	N	Control group	N
<b>Own net income per month</b>		<b>480</b>		<b>483</b>
No income	11.25%	54	15.76%	76
<3000 CHF (1000 €)	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500€)	49.17%	236	40.37%	195
>6000 CHF (>2500 €)	14.79%	71	15.32%	74
<b>Desired profession</b>		<b>488</b>		<b>482</b>
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
<b>Degree of health-related limitations in career choice</b>		<b>486</b>		<b>466</b>
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
<b>Estimation of adequacy of job qualification</b>		<b>459</b>		<b>453</b>
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
<b>Professional experience</b>		<b>487</b>		<b>474</b>
less than 5 years	18.89%	92	32.70%	155
between 5 and 10 years	25.87%	126	21.10%	100
more than 10 years	55.24%	269	46.20%	219
<b>Duration of current employment</b>		<b>442</b>		<b>439</b>
less than 1 year	14.25%	63	20.27%	89
between 1 and 5 years	40.72%	180	41.69%	183
between 5 and 10 years	22.17%	98	18.91%	83
more than 10 years	22.85%	101	19.13%	84
<b>Work-related stress level</b>		<b>460</b>		<b>465</b>
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24
3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66

7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

312

313 Spearman correlation between professional experience and length of time in the  
314 current employment was  $r = 0.490$  ( $p < 0.001$ ).

315

316 Associations between endometriosis and work outcomes after adjustment for age,  
317 nationality, number of pregnancies, and occupation are presented in Table IIIb.

318

319 **Table IIIb: Associations between endometriosis and parameters of pro-**  
320 **fessional life including the proportion of variance explained by the disease**

Outcome	Reference category	Unadjusted OR (95% CI)	Adjusted OR** (95% CI)	R <sup>2</sup>	p**
Own income	1 point increase <sup>a</sup>	1.26 (0.99; 1.60)	1.09 (0.81; 1.47)	0.004	p=0.572
Desired profession	Yes	0.47 (0.34; 0.65)*	0.45 (0.31; 0.66)*	0.026	p<0.001
	Partially	0.67 (0.45; 1.00)	0.65 (0.42; 1.02)		
	No	Ref.			
Degree of health-related limitations in career choice	1 point increase <sup>b</sup>	2.92 (2.10; 4.04)*	3.08 (2.14; 4.42)*	0.062	p<0.001
Estimation of adequacy of job qualification	too high	1.82 (1.18; 2.80)*	1.47 (0.92; 2.36)	0.011	p=0.387
	too low	1.25 (0.89; 1.77)	1.21 (0.83; 1.77)		
	adequate	Ref.			
Professional experience	1 point increase <sup>c</sup>	1.63 (1.28; 2.07)*	2.29 (1.73; 3.03)*	0.019	p<0.001
Duration of current employment	1 point increase <sup>d</sup>	1.36 (1.07; 1.74)	1.65 (1.26; 2.16)*	0.008	p<0.001
Work-related stress level	1 point increase <sup>e</sup>	1.50 (1.20; 1.89)*	1.17 (0.91; 1.50)	0.014	p=0.210

321

\* Statistically significant at Bonferroni corrected  $\alpha=0.007$ 

322

\*\* Adjusted for age, time since diagnosis, nationality, number of pregnancies, and occupation

323

<sup>a</sup> Scale: 1= $\leq$ 3000 CHF (1000 EUR), 2=3001-6000 CHF (1001-3000 EUR), 3= $\geq$ 6000 CHF (>3000 EUR) per month

324

<sup>b</sup> Scale: 1="not at all", 2="moderately", 3="strongly"

325

<sup>c</sup> Scale: 1= $<$ 5 years, 2=5-10 years, 3= $\geq$ 10 years

326

<sup>d</sup> Scale: 1= $<$ 1 year, 2=1-5 years, 3=5-10 years, 4= $\geq$ 10 years

327

<sup>e</sup> Scale: 0="no stress at all" – 10="extreme stress"

328

329 Results of the main outcome measures are highly significant. However, except for  
330 health influences on career choice ( $R^2 = 0.062$ ), the proportion of variance explained



1  
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3 331 by each factor was small (all  $R^2 < 0.027$ ). Excluding participants who are members of  
4  
5 332 self-help groups did not alter the results, except that the multivariate analysis for  
6  
7 333 professional experience was attenuated to  $OR=1.49$  ( $p = 0.003$ ), whereas the  
8  
9 334 adjusted association with duration of the current employment was diminished to an  
10  
11 335 insignificant  $OR = 1.17$  ( $p = 0.231$ ).

12  
13  
14 336

15  
16 337 The intensity of reported health-related limitations in career choice was independent  
17  
18 338 from rASRM-stage ( $\chi^2$ , 16.51,  $df = 12$ ,  $p = 0.169$ ), but associated with the occurrence  
19  
20 339 of chronic pain ( $\chi^2$ , 34.39,  $df = 4$ ,  $p < 0.001$ ) as well as with the frequency of pain ( $\chi^2$ ,  
21  
22 340 25.62,  $df = 8$ ,  $p = 0.001$ ).

23  
24  
25 341

26  
27 342 Chronic pain was also associated with higher levels of stress at work, even if the  
28  
29 343 difference of means was rather small (6.61 vs 5.47,  $SD = 2.39/ 2.49$ ,  $p < 0.001$ ).

30  
31 344 Intraoperative findings of spread of endometriosis lesions showed varying  
32  
33 345 associations with health-related limitations in career choice: having endometriosis  
34  
35 346 lesions at the pelvic wall ( $\chi^2$ , 11.14,  $df = 4$ ,  $p = 0.025$ ) or in the sacrouterine  
36  
37 347 ligaments ( $\chi^2$ , 13.51,  $df = 4$ ,  $p = 0.009$ ) was significantly associated with greater  
38  
39 348 limitations in career choice, while such an outcome could not be found for localization  
40  
41 349 in the vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of  
42  
43 350 stress at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50,  
44  
45 351  $SD = 2.46/ 2.48$ ,  $p = 0.001$ ), but not with other intraoperative findings.

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### 50 353 **Work impairment and compensatory mechanisms**

51  
52 354 Asked about the amount of sick leave due to endometriosis during the last month,  
53  
54 355 78.1% of the women of the case group reported no sick leave, 8.5% reported one to

356 three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and  
357 8.1% reported two to four weeks.

358 Altogether, 13.1% of endometriosis patients used one week or more of overtime or  
359 vacation when they felt too sick to work. Furthermore, 75.5% of women with  
360 endometriosis reported to have gone to work during the previous month in spite of  
361 severe pain. Asked about the previous year, 89.2% of women affirmed to have  
362 worked despite pain. Out of these women, 89.8% noted a loss of work productivity,  
363 with 65.1% reporting strong or very strong limitations when symptoms were severe.  
364 On days with minimal endometriosis symptoms, 75.3% still felt some degree of loss  
365 of productivity.

366 A minority of women with endometriosis reported working part time (10.3%) or giving  
367 up work entirely (5.8%) due to their disease (n = 445).

### 368 369 **Association of endometriosis-related symptoms with sick leave and** 370 **productivity loss**

371 We then examined whether different endometriosis symptoms were related to  
372 absenteeism and impaired work productivity (Table IV).

373  
374 **Table IV: Association of endometriosis-related symptoms to sick leave and**  
375 **productivity loss in the last month**  
376

Predictor		Sick leave <sup>a</sup>			Productivity loss <sup>b</sup>		
		OR** (95% CI)	R <sup>2</sup>	p	OR** (95% CI)	R <sup>2</sup>	p**
Chronic pain	Yes	3.52 (2.02; 6.13)*	0.072	p<0.001	3.08 (2.11; 4.50)*	0.087	p<0.001
	No	Ref.			Ref.		
Frequency of pain	Daily	2.82 (1.47; 5.39)*	0.053	p=0.002	1.81 (1.05; 3.12)	0.040	p=0.032
	>1 per week	1.40 (0.66; 2.97)			0.76 (0.42; 1.38)		
	≤1 per week	Ref.			Ref.		
Frequency of fatigue	Frequently	3.50 (1.76; 6.94)*	0.073	p<0.001	3.99 (2.49; 6.39)	0.107	p<0.001
	Sometimes	1.15 (0.50; 2.64)			1.44 (0.86; 2.41)		
	Rarely	Ref.			Ref.		

Psychological symptoms <sup>c</sup>	Yes	3.03 (1.77; 5.18)*	0.061	p<0.001	2.90 (1.98; 4.23)*	0.082	p<0.001
	No	Ref.			Ref.		

377 \* Statistically significant at Bonferroni corrected  $\alpha=0.01$

378 \*\* Adjusted for age and time since diagnosis

379 <sup>a</sup> Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days

380 <sup>b</sup> Refers to current maximal impairments; Scale: 1="not at all/ little", 2="moderately/ strong", 3="very strong"

381 <sup>c</sup> depressive mood/ anxiety/ reduced resilience of more than three months

382

383 All four predictor variables were significantly associated with sick leave during the  
 384 previous four weeks. The occurrence of chronic pain as well as concomitant  
 385 psychological symptoms were associated with significantly higher degrees of  
 386 perceived productivity loss, but the extent of the effect was modest and the effect  
 387 accounted for less than 11% of variance explained. Including age and time since  
 388 diagnosis as potential confounders did not alter the results. Likewise, the factor of  
 389 different localisations of endometriosis was not associated with sick leave or  
 390 productivity loss (all  $p > 0.05$ ).

391

392

## 393 Discussion

394

395 Endometriosis is associated with impairment of professional activity: women  
 396 diagnosed with endometriosis showed a lower likelihood of working in their desired  
 397 profession and stronger health-related limitations in their career decisions. In  
 398 contrast, they had professional experience of longer durations. All of these main  
 399 outcomes were not reported previously and open new insights into the professional  
 400 life of women with endometriosis.

401 Endometriosis-associated symptoms and symptom characteristics were moderately  
 402 related to sick leave and loss of productivity, but in contrast to our expectations,  
 403 endometriosis was not associated with increased work-related stress levels.

404

405 Education level and salaries did not differ significantly between case and control  
406 groups (Table I); this is a result that has been described previously.<sup>13</sup> Other studies,  
407 however, reported serious effects of endometriosis on education level, especially on  
408 tertiary formation.<sup>8 20</sup> These contrasting findings might result from differences in study  
409 groups, eg with regard to the onset of disease symptoms in relation to education,  
410 professional training and professional activity. Many studies report an average age of  
411 first symptoms between 20 and 29 years,<sup>6 26-28</sup> ie an age at which most women have  
412 completed professional training. Other authors reported an earlier onset of disease  
413 symptoms,<sup>29</sup> and emphasized that endometriosis in adolescent girls was an  
414 underestimated problem.<sup>28 30 31</sup> An additional factor responsible for a different  
415 association between endometriosis and education vs. professional performance  
416 might be a higher tolerance for sick leave and impaired energy levels in a school or  
417 university setting compared to in paid employment.

418

419 Health issues are important criteria in career choice, and women diagnosed with  
420 endometriosis do work less often in their desired profession. However, women with  
421 endometriosis reported a higher quality of experience in the current profession (Table  
422 IIIb). Professional experience and the length of time a woman is working with the  
423 current employer are highly correlated, and the difference between groups for time  
424 with the same employer remained no longer significant when women attending a self-  
425 help group were excluded. These results can be interpreted positively in the sense  
426 that women with endometriosis were successful in carefully choosing a long-term  
427 profession. The lower number of children in women with endometriosis may also  
428 contribute to a professional experience of longer duration.

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3 430 Several authors reported elevated levels of general<sup>32 33</sup> as well as emotional<sup>21</sup>  
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5 431 distress in women diagnosed with endometriosis. This first study on work-specific  
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7 432 stress in endometriosis affected women produced results in contrast to our  
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9 433 expectations. Even though women reported that they sometimes went to work  
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11 434 despite endometriosis-associated pain, women with endometriosis did not  
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13 435 experience higher work-related stress levels than the control women; but within the  
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15 436 group of women with endometriosis, those with chronic pain reported significantly  
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17 437 higher work-related stress than those without pain. We investigated women whose  
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19 438 initial diagnosis was up to 20 years ago; these women may have meanwhile found an  
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21 439 occupation meeting their needs, and superiors and colleagues may have adapted to  
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23 440 their sometimes reduced availability for work. Also, the fact that work can be a source  
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25 441 of distraction and of self-esteem for individuals suffering from a chronic disease<sup>34</sup>  
26  
27 442 may offset stressful situations.  
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30  
31 443 According to our results and those of others,<sup>29</sup> women affected by endometriosis  
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33 444 compensate for their health-related restrictions at work by using overtime or vacation  
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35 445 for absences as well as by saving energy for work through reduction of leisure time  
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37 446 activities.  
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42 448 Despite these personal efforts to adapt to an adverse situation, productivity loss<sup>9 15</sup>  
43  
44 449 and sick leave<sup>9 10</sup> are relevant issues for many women diagnosed with endometriosis.  
45  
46 450 Average loss of work time per week (absenteeism) due to endometriosis is reported  
47  
48 451 to be between 4.4 and 7.4 hours.<sup>9 10</sup> In our study, chronic pain, the frequency of pain,  
49  
50 452 fatigue, and psychological symptoms, such as self-reported depression and anxiety,  
51  
52 453 were significantly - but with small effect sizes - related to taking more sick leave  
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54 454 (Table IV). Productivity loss at work due to endometriosis-related symptoms was  
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56 455 described to be high or very high – depending on the current severity of symptoms –  
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3 456 by up to 65% of women in the present study. Struggles to fulfil normal demands of  
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5 457 work might be exacerbated by the side effects of treatment, for example by dizziness  
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7 458 from strong pain killers.<sup>18 19</sup> Although, the majority of women affected with  
8  
9 459 endometriosis seemed to be able to compensate for disease-related difficulties at  
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11 460 work and to realize successful long-term professional activity, 16.2% of the women  
12  
13 461 nevertheless reduced or even gave up work entirely due to endometriosis-related  
14  
15 462 symptoms; this is a situation that has been observed also by others.<sup>13</sup> Furthermore, a  
16  
17 463 very similar percentage of women with endometriosis and control women worked part  
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19 464 time, even though women diagnosed with endometriosis remained childless more  
20  
21 465 often. Such decisions may result from feeling pressured to reduce or quit work when  
22  
23 466 employers know about a chronic disease such as endometriosis.<sup>8 20</sup> More flexible  
24  
25 467 work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted  
26  
27 468 physical demands, the possibility to lie down, and the existence of bathrooms nearby  
28  
29 469 are seen to be helpful resources for successful professional performance in women  
30  
31 470 with endometriosis.<sup>19 20</sup>

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37 472 As for the relationship between rASRM stage and endometriosis-associated  
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39 473 symptoms,<sup>1 3</sup> none of the parameters evaluating professional activity showed any  
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41 474 significant association with rARSM stage. Testing the association between different  
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43 475 intraoperative findings of endometriotic lesions and work outcomes showed  
44  
45 476 inconsistent results. In contrast, most outcome measures were related to the  
46  
47 477 occurrence and frequency of chronic pain; this result is supported by other studies on  
48  
49 478 endometriosis,<sup>10 15</sup> as well as on other chronic pain conditions such as migraine or  
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51 479 fibromyalgia.<sup>35 36</sup> Even if the effect size of pain on work in this study is limited,  
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55 480 findings support the relevance of pain management for satisfactory work  
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3 481 performance. Exhaustion, either as a symptom of endometriosis or as a frequent  
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5 482 comorbidity,<sup>37</sup> interfered with professional activity in this as well as in other studies.<sup>19</sup>  
6  
7 483 In summary, women with endometriosis strive for normality at their work place, even  
8  
9 484 if it is associated with reduced professional flexibility or with giving up the desire for  
10  
11 485 another profession.  
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14 486

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16 487 This study presents one of the largest samples investigating the association between  
17  
18 488 endometriosis and professional life and it is one of the very few studies providing a  
19  
20 489 control group. Study participants were recruited in university hospitals, in district  
21  
22 490 hospitals and in doctors' practices in order to collect a representative sample. The  
23  
24 491 pair matching with regard to age and ethnic background reduced the confounding  
25  
26 492 effect of these factors. A meticulous review of all surgical records by the same  
27  
28 493 investigator (AKS) ensured high data quality with regard to diagnosis and  
29  
30 494 classification of endometriosis. The response rate of 64.1% in the case group is in  
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32 495 the upper level of comparable studies,<sup>8 9</sup> whereas the response rate of 35.8% in the  
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34 496 control group is comparatively low. We cannot exclude that women with a particularly  
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36 497 high work load refrained from study participation; however, such an effect is equally  
37  
38 498 relevant in women diagnosed with endometriosis and in controls. The higher  
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40 499 response rate in women with endometriosis supports the fact that such an  
41  
42 500 association does not represent a particular problem for members in this group.  
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45  
46 501 Given the methodology of a self-reported questionnaire answered retrospectively,  
47  
48 502 distortions in the sense of falsely or overly attributing dissatisfaction on the job to  
49  
50 503 endometriosis cannot be excluded. By addressing questions on professional activity  
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52 504 either current or in the period just prior to study participation, we tried to reduce recall  
53  
54 505 bias. As we included only patients with a confirmed diagnosis of endometriosis, and  
55  
56 506 as such a confirmation can be provided only by surgery, there may be referral bias.  
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3 507 For example, affected but asymptomatic women and symptomatic women who do  
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5 508 not have access to or refused surgery might have been excluded. In contrast,  
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7 509 asymptomatic women with endometriosis might have been included in the control  
8  
9 510 group which would result in underestimation of results. As we have no differentiated  
10  
11 511 information on symptoms resulting from diseases other than endometriosis, in both  
12  
13 512 groups further confounders might be present; this would also result in  
14  
15 513 underestimation of our findings. A comparison group for the questions of sick leave  
16  
17 514 and productivity loss at work would have been beneficial. However, analysis of  
18  
19 515 gradual impact of different endometriosis-related symptoms on these two outcomes  
20  
21 516 allowed for indirect conclusions on the association between endometriosis and  
22  
23 517 reduced working ability, as well as basic data to design future studies.  
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## 520 **Conclusion**

521 Even if most measured effect sizes of associations between endometriosis and  
522 individual parameters of working life were small, the study confirms a burdensome  
523 influence of the disease on the working life of women affected by endometriosis.  
524 Therefore, medical support should address such issues in order to support women in  
525 adjusting their professional choices and professional development to individual  
526 endometriosis-related conditions.

527

528

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8

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13  
14 538 **Authors roles**

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16 539 MLS: collection of data on site in Solothurn and Schaffhausen, interpretation of data,  
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18 540 drafting and finalization of the manuscript

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20 541 MPH: statistical analysis, interpretation of data, finalization of manuscript

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22 542 AKS: investigator, collection of data on site in Winterthur, Switzerland, verification of  
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24 543 surgical reports, finalization of the manuscript

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9 561 finalization of the manuscript

10  
11 562 DF: concept of study, investigator on site in Zurich, Switzerland, interpretation of  
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13 563 data, finalization of manuscript

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17 565 Switzerland, collection and analysis of data, preparation and finalization of  
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19 566 manuscript

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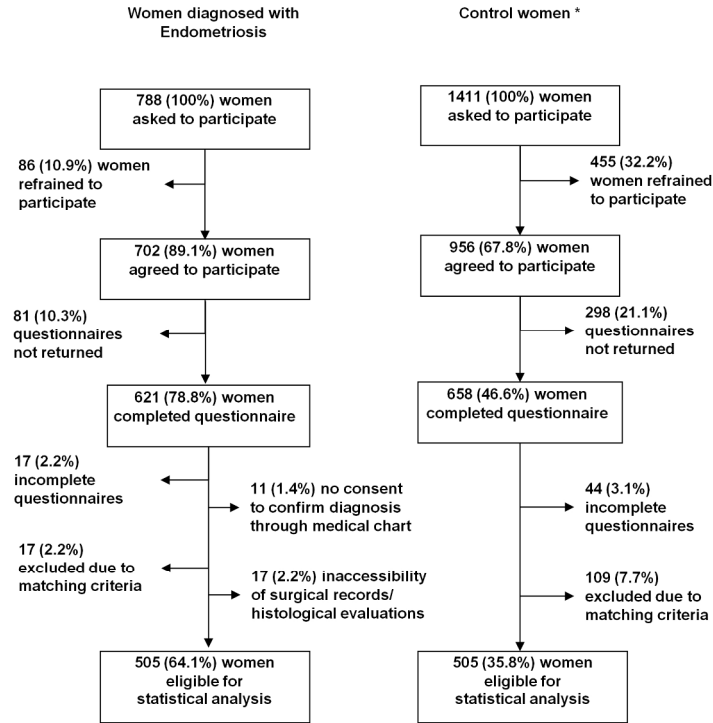
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29 668 **Figure legends**

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33 670 Fig 1.: Recruitment of study participants  
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Flow chart I. Recruitment of study participants



\* women presenting for routine gynaecological care or benign gynaecological surgery

190x274mm (284 x 284 DPI)

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8/9
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	7



		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Does endometriosis affect professional life? – a matched case-control study

Journal:	<i>BMJ Open</i>
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<b>Primary Subject Heading</b>:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

SCHOLARONE™  
Manuscripts

# 1 Does endometriosis affect professional life? – 2 a matched case-control study

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1  
2  
3 35 **Abstract**  
4

5 36 **Objectives:** Endometriosis is a gynaecological disease most commonly causing  
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8 37 severe and chronic pelvic pain as well as an impaired quality of life. The aim of this  
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11 38 study was to investigate if and how endometriosis affects choices regarding  
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13 39 professional life as well as the quality of daily working life.  
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16 40 **Design, setting, and participants:** In the context of a multicentre case-control  
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19 41 study, we collected data from 505 women with surgically/histologically confirmed  
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21 42 diagnosis of endometriosis and 505 matched controls. Study participants were  
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23 43 recruited prospectively in hospitals and doctors' practices in Switzerland, Germany,  
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25 44 and Austria. Using a detailed questionnaire, the study investigated work-life and  
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27 45 career choices of study participants.  
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30 46 **Main outcome measures:** Associations between endometriosis/ disease symptoms  
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32 47 and limitations in career development as well as ability to work.  
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34 48 **Results:** Women with endometriosis were less often able to work in their desired  
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37 49 profession than women from the control group (adjusted OR=1.84, 95%-CI: 1.15-  
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39 50 2.94,  $R^2=0.029$ ,  $p=0.001$  and they had to take health-related limitations into  
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41 51 consideration in their career decisions to a significantly higher degree than women in  
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43 52 the control group (aOR=4.79, 95%-CI: 2.30-9.96,  $R^2=0.063$ ,  $p<0.001$ ). Among  
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45 53 women with endometriosis, chronic pain was significantly associated with increased  
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47 54 sick leave (OR=3.52, 95%-CI: 2.02-6.13,  $R^2=0.072$ ,  $p<0.001$ ) as well as with loss of  
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49 55 productivity at work (OR=3.08, 95%-CI: 2.11-4.50,  $R^2=0.087$ ,  $p<0.001$ ).  
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53 56 **Conclusions:** Endometriosis is associated with impairment of professional life, in  
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56 57 particular with regard to career choices. Further research to develop strategies to  
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3 58 support endometriosis-affected women in realizing professional opportunities is  
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5 59 recommended.

### 60 **Strengths and limitations of this study**

61 This study presents one of the largest samples investigating the association between  
62 endometriosis and professional activity. It is one of the first studies in this field to  
63 provide a matched control group.

64 Recruitment of study participants in university hospitals, in district hospitals and in  
65 private doctors' practices ensured a representative sample.

66 Validation of diagnosis and stage of endometriosis by case reports provided high  
67 data quality.

68 Given the design of the study (using a self-reported questionnaire answered  
69 retrospectively), distortions in the sense of false or excessive attribution of  
70 professional dissatisfaction to endometriosis cannot be excluded.

71 As we did not investigate diseases or symptoms that may also have had an impact  
72 on professional life in the control group, results may be underestimated.

73

### 74 **Trial registration number**

75 Clin.trial.gov: Endo\_QOL NCT02511626

76

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78 This research received no specific grant from any funding agency in the public,  
79 commercial, or not-for-profit sectors.

80

### 81 **Conflict of interest**

82 The authors do not have any conflicts of interest.

83

## 84 **Data sharing statement**

85 The data set is available on request from the corresponding author.

86

87 **Key words:** Endometriosis, work, professional life, stress, career choice

88

89

## 90 **Introduction**

91

92 Endometriosis is a gynaecological disease defined by the presence of endometrium-  
93 like tissue outside the uterine cavity.<sup>1</sup> The prevalence of the disease among women  
94 of reproductive age is estimated to be between 8 and 10%.<sup>2,3</sup>

95 Women suffering from endometriosis experience most commonly one or more of the  
96 following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia,  
97 pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea,  
98 as well as reduced fertility and chronic fatigue.<sup>4,5</sup> Numerous and severe symptoms,  
99 the chronicity of the disease, side effects of therapies as well as diagnostic delays<sup>6,7</sup>  
100 significantly affect women's overall quality of life, including professional performance,  
101 and place high demands on the treating physicians.<sup>8,9,10</sup> For most patients, available  
102 treatment options, such as analgesics, various hormonal therapies, and radical lapa-  
103 roscopy<sup>1</sup> are often not curative and are associated with significant side effects.<sup>8,11</sup>

104 Consequently, disease symptoms, especially endometriosis-related pain and fatigue,  
105 may disturb the development and realization of long-term goals such as a  
106 professional career<sup>12</sup> and may make it difficult to meet the demands of a job. About  
107 40% of women with endometriosis report impaired career growth due to  
108 endometriosis,<sup>9</sup> and about 50% experience a decreased ability to work due to their  
109 chronic disease.<sup>8,13</sup> Differentiated knowledge on the nature of such limitations and in

1  
2  
3 110 particular on how adjustments to professional life can be made to improve  
4  
5 111 professional performance is currently lacking.

6  
7 112 The quality of working life is a major aspect in quality of life overall,<sup>14</sup> which in turn is  
8  
9 113 the most important predictor of total cost of disease.<sup>15</sup> About 66% to 75% of the total  
10  
11 114 costs of endometriosis arise from reduced ability to work and not from direct costs of  
12  
13 115 treatment.<sup>15 16</sup> Being able to work in a desired occupation may not only have a strong  
14  
15 116 impact on a woman's financial situation and on the perception of and attitude toward  
16  
17 117 daily work, but can also be an important health factor. For example, unsatisfactory  
18  
19 118 work and limited possibilities for change are associated with increased levels of  
20  
21 119 headache, fatigue and depressed mood.<sup>17</sup>

22  
23  
24 120 Frequent sick leave and reduced work productivity can put affected women under  
25  
26 121 observation by superiors and under greater pressure to deliver full performance.<sup>18 19</sup>

27  
28 122 The rather intimate and gender-specific nature of the most common endometriosis  
29  
30 123 symptoms tends to make affected women feel embarrassed.<sup>20</sup> Consequently, some  
31  
32 124 women may avoid discussing endometriosis-related problems with superiors and  
33  
34 125 colleagues, particularly if the superiors and colleagues are male.<sup>20 21</sup> Due to the  
35  
36 126 invisibility of their disease, women can be easily perceived as malingerers.<sup>20</sup>

37  
38 127 Therefore, medical professionals need to know how the symptoms of endometriosis  
39  
40 128 can affect daily working life and professional development, notably because  
41  
42 129 endometriosis-affected women repeatedly underline their wish for comprehensive  
43  
44 130 information<sup>20 22 23</sup> and advice in managing their disease in daily life,<sup>22 23</sup> instead of  
45  
46 131 isolated treatment of endometriosis symptoms.<sup>20 22 23</sup> A better understanding of  
47  
48 132 endometriosis and its impacts on any aspect of life - including professional activity -  
49  
50 133 not only by medical professionals but also in society and politics would help affected  
51  
52 134 women and their families to reduce negative consequences of the disease. However,  
53  
54 135 research on quantitative and qualitative impairment of working life as the necessary

1  
2  
3 136 background for offering adequate support and interventions is scarce and relies  
4  
5 137 mainly on interview-based studies with small samples of affected women<sup>19 20</sup>; there is  
6  
7 138 only one other study that uses a control group.<sup>10</sup> In addition, work-related stress in  
8  
9 139 women diagnosed with endometriosis has not been investigated yet.

10  
11 140 Therefore, it was the aim of the present study to investigate parameters of working  
12  
13 141 life of a larger number of endometriosis-affected women, and compare findings with  
14  
15 142 those of a matched control group. We investigated (i) perceived health-related  
16  
17 143 limitations in career decisions; (ii) quality of the current work situation; and (iii) the  
18  
19 144 association between endometriosis-related disease symptoms and work  
20  
21 145 performance.  
22  
23  
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25

26 146

## 27 147 **Material and Methods**

28  
29 148

### 30 149 **Study design**

31  
32 150 The study is designed as a multicentre case-control study. Main outcome measures  
33  
34 151 are health limitations in career choice as well as quality and stability of the current  
35  
36 152 work situation. Secondary outcome measures investigate the impact of different  
37  
38 153 symptoms as well as localisation of endometriosis on sick leave and loss of  
39  
40 154 productivity. The study has been conducted and reported applying the criteria of the  
41  
42 155 STROBE Statement.<sup>24</sup>  
43  
44  
45  
46

47 156

### 48 157 **Recruitment**

49  
50 158 Recruitment of study participants is shown in Figure I. To detect a 10% difference  
51  
52 159 between cases and controls with an alpha of 0.05, and a power of 0.8 a sample size  
53  
54 160 of 387 participants in each group is needed. With the inclusion of 505 participants in  
55  
56  
57  
58  
59  
60



1  
2  
3 161 both groups we consequently reached very high power, for example 99.1 for the  
4  
5 162 detection of differences in desired profession or 99.7 for health-related limitations in  
6  
7 163 career choice. Study participants were recruited prospectively for a research project  
8  
9 164 on quality of life including professional activity in endometriosis-affected women  
10  
11 165 compared to control women. Recruitment took place between January 2010 and  
12  
13 166 December 2015 at the following hospitals and associated doctors' offices in  
14  
15 167 Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli  
16  
17 168 Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen,  
18  
19 169 Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes Humboldt  
20  
21 170 Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital Aachen,  
22  
23 171 and the University Hospital Graz. In doctors' offices one or several gynecologists  
24  
25 172 work together in a medical unit; district hospitals offer tertiary care associated with a  
26  
27 173 university.

28  
29 174 Healthcare professionals carried out the recruitment of all study participants via direct  
30  
31 175 approach. The study was explained to the respondents and information about the  
32  
33 176 voluntary nature of participation as well as anonymity of data in reports and  
34  
35 177 publications was provided. Each participant received a detailed written description of  
36  
37 178 the study and signed informed consent. Participants were given all documents and a  
38  
39 179 return envelope.

40  
41 180 Inclusion criteria: All study participants had to be between 18 and 50 years old. For  
42  
43 181 the case group, women with surgically and histologically diagnosed endometriosis  
44  
45 182 were included irrespective of stage, location of lesions, and severity and profile of  
46  
47 183 symptoms. Only data sets with at least 80% of answers for main and secondary  
48  
49 184 outcome measures were included.

50  
51 185 Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic,  
52  
53 186 mental or psychological impairments that might affect their ability to understand and

187 to complete the questionnaire.

188 The most frequent reasons reported for not participating were lack of time and the  
189 intimate nature of some of the questions. To maximize the return rate, women were  
190 reminded to complete and return the questionnaire after one month and after three  
191 months.

192 A smaller segment of the case group (N=74, 66 of which could be included in the  
193 final analysis (13.1% of total case group)) was recruited through different self-help  
194 groups for endometriosis patients (in Germany only). Education levels and family  
195 incomes in this cohort are similar to those in the main group. However, the women in  
196 this cohort were significantly older than those in the hospital group ( $42.45\pm 6.03$   
197 versus  $37.02\pm 7.21$  years,  $p<0.001$ ), showed a longer time since primary diagnosis  
198 ( $82.11\pm 8.36$  versus  $37.20\pm 44.00$  months,  $p<0.001$ ), and presented at the time of the  
199 study a significantly higher stage of disease ( $p=0.013$ ).

200 Control women were recruited during regular annual or biennial gynaecological  
201 consultations, as part of standard healthcare in the three countries where recruitment  
202 took place. In addition, women during hospital stays because of temporary mild  
203 benign gynaecological problems other than endometriosis were invited to participate  
204 in the study. Each control woman was matched to a woman diagnosed with  
205 endometriosis for age ( $\pm 3$  years) and ethnic background, i.e. Caucasian or not (pair  
206 matching).

207

## 208 **Questionnaire**

209 The structured self-administered questionnaire for the total study on quality of life  
210 contained 390 questions for all participants and 90 additional specific questions for  
211 women diagnosed with endometriosis. It is structured in different chapters, one of  
212 which is professional life. Further chapters covered questions regarding life style;

1  
2  
3 213 general wellbeing; general, gynaecological, and medical history; childhood  
4  
5 214 experiences; sexuality and partnership. Women diagnosed with endometriosis were  
6  
7 215 additionally asked to provide detailed information on the diagnosis and treatment of  
8  
9 216 endometriosis, symptoms of endometriosis, sick leave, and productivity loss due  
10  
11 217 specifically to endometriosis. Wherever possible we used internationally validated  
12  
13 218 questionnaires. Modified versions of the Brief Pain Inventory<sup>25</sup> and the Pain Disability  
14  
15 219 Index<sup>26 27</sup> served to evaluate pain. For several questions about professional life as for  
16  
17 220 occupation, sick leave and productivity loss, we used similar reporting methods the  
18  
19 221 WPAI<sup>28</sup> suggests, but extended the time period of reporting from only seven days in  
20  
21 222 the WPAI to four weeks and one year. Level of education was measured with defined  
22  
23 223 categories following the recommendation to use meaningful benchmarks of  
24  
25 224 educational attainment rather than a continuous scale in years.<sup>29</sup> In order to capture  
26  
27 225 the professional situation of women diagnosed with endometriosis as close to reality  
28  
29 226 as possible a interdisciplinary research team including specialists for minimally  
30  
31 227 invasive endometriosis-surgery, for gynaecological endocrinology and for gynaeco-  
32  
33 228 psychosomatic medicine added their clinical experience and evaluated systematically  
34  
35 229 what they had learned from individual patients. On this background specific questions  
36  
37 230 like on working despite pain or on using overtime or holidays to compensate for sick  
38  
39 231 leave were added. The first version of our questions on professional activity was than  
40  
41 232 revised by the governing body of the German self-help groups in order to map the  
42  
43 233 questions to the situations reported by women with endometriosis and to avoid using  
44  
45 234 questions, which do not correctly depict the specific situation in the context of  
46  
47 235 endometriosis.  
48  
49 236 The analysis presented in this paper was based on answers to the following  
50  
51 237 questions asked to the case as well as to the control group: nationality (German,  
52  
53 238 Swiss, Austrian, other [with the possibility of entering nationality]), age (years),  
54  
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2  
3 239 marital status (married/cohabiting/single), highest achieved education level (lower  
4  
5 240 school education, high school education, apprenticeship, university degree, no formal  
6  
7 241 education, other), current own monthly net income (six choices for responses ranging  
8  
9 242 from none to >2500 Euros for participants in Germany and Austria and from none to  
10  
11 243 >6000 Swiss francs for participants in Switzerland), numbers of pregnancies of more  
12  
13 244 than 24 weeks of gestation. Women were asked to report their levels of current  
14  
15 245 employment (full-time/part-time/full-time housekeeping/student/registered as  
16  
17 246 unemployed) and whether they currently worked in their desired profession (yes/no).  
18  
19 247 This question does not ask about the current place of employment but on the  
20  
21 248 profession itself, e.g. for a woman who always wanted to be a teacher, is she now  
22  
23 249 able to work as a teacher? They were asked how they perceived their level of  
24  
25 250 qualification for the currently held job (overqualified, about right, under-qualified),  
26  
27 251 length of professional experience (<5 years, 6-10 years, and >10 years), years  
28  
29 252 working with the current employer (<1 year, 1-5 years, 6-10 years, >10 years), the  
30  
31 253 subjectively perceived influence of health-related limitations on career choice (not at  
32  
33 254 all, little, medium, strongly, exclusively) and perceived current level of stress on the  
34  
35 255 job (scale from 0=none to 10=very strong).  
36  
37 256 The analysis presented in this paper further used the following questions asked only  
38  
39 257 to women diagnosed with endometriosis: Amount of time since first symptoms of  
40  
41 258 endometriosis were noticed (<1 year ago/1 year ago/2-5 years ago/6-10 years  
42  
43 259 ago/>10 years ago), date of initial diagnosis of endometriosis (month and year),  
44  
45 260 number of surgeries related to endometriosis (1/2/3/4/5/6 or more), chronic pain  
46  
47 261 (yes/no), duration of pain (<1 year/1-3 years/4-5 years/6-10 years/11-20 years/>20  
48  
49 262 years), frequency of pain (a few times per year/a few times per month/several times  
50  
51 263 per week/once a day/several times a day/permanently), cyclic pain (yes/no),  
52  
53 264 psychological symptoms lasting more than three months estimated by the study  
54  
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3 265 participant to be related to endometriosis, such as depressive mood/anxiety/reduced  
4  
5 266 resilience (yes/no), days worked despite pain during the last month (never/1-3  
6  
7 267 days/4-7 days/1-2 weeks/2-4 weeks), frequency of fatigue or exhaustion due to  
8  
9 268 endometriosis (never/rarely/sometimes/often/very often), sick leave due to symptoms  
10  
11 269 of endometriosis (not specified) during the last month (never/1-3 days/4-7 days/1-2  
12  
13 270 weeks/2-4 weeks), sick leave due to symptoms of endometriosis in the last year  
14  
15 271 (never/1-7 days/1-2 weeks/2-4 weeks/4-8 weeks/8-12 weeks/>12 weeks), estimated  
16  
17 272 loss of productivity due to endometriosis when symptoms are at their maximum or at  
18  
19 273 their minimum respectively (no loss/a little/somewhat/high), reduction of work time  
20  
21 274 due to endometriosis (no reduction/reduction of 25%/50%/75%), and giving up  
22  
23 275 employment entirely due to endometriosis (yes/no). (Chronic pelvic pain included  
24  
25 276 cyclic as well as non-cyclic pelvic pain.)

26  
27  
28 277 The study was registered at clinicaltrials.gov (NCT 02511626), where further details  
29  
30 278 on the complete questionnaire are available.  
31  
32

33 279

### 34 280 **Verification of diagnosis and stage of endometriosis**

35 281 To verify diagnosis and obtain information about localization of endometriosis  
36  
37 282 lesions, surgical records as well as the histological diagnosis of each patient and  
38  
39 283 each intervention were collected from medical charts. Stage was classified according  
40  
41 284 to the revised Classification of the American Society for Reproductive Medicine  
42  
43 285 (rASRM).<sup>30</sup>  
44  
45

46 286

### 47 287 **Ethical approval**

48  
49  
50 288 The study was approved by the Swiss ethics commission as well as by the ethics  
51  
52 289 boards of participating hospitals. This study followed the guidelines of the World  
53  
54 290 Medical Association Declaration of Helsinki 1964, updated in October 2013.  
55  
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3 2914  
5 292 **Patient and Public Involvement statement**

6  
7 293 Questions for this study were selected in cooperation with endometriosis self-help  
8  
9 294 groups. Other than in the self-help groups patients were not involved in the  
10  
11 295 recruitment and conduct of the study. All interested study participants receive the  
12  
13 296 publications resulting from the study. Publications are also sent to the governing  
14  
15 297 body of the self-help groups.  
16

17  
18 29819  
20 299 **Statistical analysis**

21  
22 300 Differences in sample characteristics between study groups were computed with  
23  
24 301 either independent sample t-tests for continuous variables or Pearson  $\chi^2$ -tests for  
25  
26 302 categorical variables. To test associations between study groups and characteristics  
27  
28 303 of professional life, we conducted a series of binomial logistic regression. The study  
29  
30 304 group, i.e. women with endometriosis as opposed to controls without endometriosis,  
31  
32 305 was included as the dependent variable. To test association between symptoms of  
33  
34 306 endometriosis and work outcomes in women with endometriosis, we conducted a  
35  
36 307 series of ordinal logistic regression, entering work outcomes as the dependent  
37  
38 308 variable. The proportion of variance explained based on the study group was  
39  
40 309 indicated by Nagelkerke's pseudo  $R^2$ . Sample characteristics that differed  
41  
42 310 significantly between study groups were statistically adjusted for by including them  
43  
44 311 simultaneously as covariates. Initially,  $\alpha$  was set at 5%, but we applied Bonferroni  
45  
46 312 correction to adjust the significance level  $\alpha$  for multiple testing. All analyses were  
47  
48 313 conducted with SPSS version 24 for Windows.  
49

50  
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52 31453  
54  
55 315 **Results**56  
57 316  
58  
59  
60

## 317 Characteristics of study groups and possible confounders

318 A comparison of socio-epidemiological parameters between women with  
 319 endometriosis and control women is presented in Table I. Significant variables, eg  
 320 nationality, pregnancies, and paid employment, were included as covariates in  
 321 subsequent analyses on case-control effects.

322  
 323 **Table I: Descriptive statistics and group comparisons**

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	p=0.344 <sup>a</sup>
Nationality	Swiss	N=211 (42.2%)	N=285 (57.3%)	p<0.001 <sup>b</sup>
	German	N=244 (48.8%)	N=161 (32.4%)	
	Others	N=45 (9.0%)	N=51 (10.3%)	
Marital status	Married/ Cohabiting	N=420 (83.3%)	N=397 (79.4%)	p=0.109 <sup>b</sup>
	Single	N=84 (16.7%)	N=103 (20.6%)	
Pregnancies >24 weeks	0	N=331 (70.6%)	N=245 (50.9%)	p<0.001 <sup>b</sup>
	1	N=83 (17.7%)	N=80 (16.6%)	
	≥2	N=55 (11.7%)	N=156 (32.4%)	
Education level <sup>c</sup>	Low	N=71 (14.4%)	N=74 (14.7%)	p=0.990 <sup>b</sup>
	Medium	N=245 (49.6%)	N=249 (49.4%)	
	High	N=178 (36.0%)	N=181 (35.9%)	
Paid occupation	Full-time	N=248 (49.8%)	N=206 (41.8%)	p=0.016 <sup>b</sup>
	Part-time	N=176 (35.3%)	N=186 (37.7%)	
	None	N=74 (14.9%)	N=101 (20.5%)	
Occupation among mothers <sup>d</sup> only	Full-time	N=30 (22.1%)	N=57 (23.9%)	p=0.120 <sup>b</sup>
	Part-time	N=68 (50.0%)	N=136 (57.1%)	
	None	N=38 (27.9%)	N=45 (18.9%)	

324 *Note*

325 <sup>a</sup> Independent samples t-test

326 <sup>b</sup> Pearson  $\chi^2$ -test

327 <sup>c</sup> Scale: Low="no formal education/lower school education", Medium="higher school education/apprenticeship",  
 328 High="university degree"

329 <sup>d</sup> women with at least one pregnancy >24 weeks

330

331 Disease characteristics of the endometriosis group are shown in Table II.

332 **Table II: Disease characteristics in women diagnosed with endometriosis**

Criteria	Endometriosis Group
----------	---------------------

		%	N
<b>Time since occurrence of first symptoms (N=474)</b>	<1 year	5.49%	26
	1 year	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	>10 years	42.19%	200
<b>rASRM-stage of endometriosis (N=502)</b>	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
<b>Number of endometriosis-related surgical interventions (N=505)</b>	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information <sup>a</sup>	7.33%	37
	Mean±SD	1.79±1.27	
<b>Douglas obliteration (N=503)</b>	Yes	26.6%	134
	No	73.4%	369
<b>Involvement of sacrouterine ligaments (N=503)</b>	Yes	61.4%	309
	No	38.6%	194
<b>Involvement of Douglas (N=503)</b>	Yes	72.0%	362
	No	28.0%	141
<b>Intra-abdominal adhesions (N=504)</b>	Yes	74.8%	377
	No	25.2%	127
<b>Involvement of pelvic wall (N=503)</b>	Yes	74.8%	377
	No	25.2%	127
<b>Involvement of vaginal fornix or septum rectovaginal (N=503)</b>	Yes	12.7%	64
	No	87.3%	439
<b>Endometrioma (N=502)</b>	Yes	49.0%	246
	No	51.0%	256
<b>Chronic pain (N=500)</b>	Yes	58.40%	292
	No	41.60%	208
<b>Duration of chronic pain</b>	<1 year	3.48%	10
	1-3 years	13.59%	39
	4-5 years	17.07%	49
	6-10 years	23.34%	67
	11-20 years	29.27%	84
	>20 years	13.24%	38
<b>Frequency of pain</b>	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
<b>Frequency of endometriosis-related fatigue/ exhaustion</b>	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Often	28.14%	141



	Very often	22.55%	113
<b>Psychological Symptoms due to endometriosis<sup>b</sup></b>	Yes	57.24%	261
	No	42.76%	195

333 *Note*

334 <sup>a</sup> question not answered but diagnosis of endometriosis confirmed with at least one surgical record

335 <sup>b</sup> depressive mood/anxiety/reduced resilience of more than three months

336

### 337 **Parameters of working life**

338 Parameters of professional activity in women diagnosed with endometriosis and  
339 control women are presented in Table IIIa.

340

341 **Table IIIa: Parameters of professional activity in the case and the control group**

Criteria	Endometriosis group	N	Control group	N
<b>Own net income per month</b>		<b>480</b>		<b>483</b>
No income	11.25%	54	15.76%	76
<3000 CHF (1000 EUR) <sup>a</sup>	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500 EUR) <sup>a</sup>	49.17%	236	40.37%	195
>6000 CHF (>2500 EUR) <sup>a</sup>	14.79%	71	15.32%	74
<b>Desired profession</b>		<b>488</b>		<b>482</b>
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
<b>Degree of health-related limitations in career choice</b>		<b>486</b>		<b>466</b>
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
<b>Estimation of adequacy of job qualification</b>		<b>459</b>		<b>453</b>
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
<b>Professional experience</b>		<b>487</b>		<b>474</b>
<5 years	18.89%	92	32.70%	155
5-10 years	25.87%	126	21.10%	100
>10 years	55.24%	269	46.20%	219
<b>Duration of current employment</b>		<b>442</b>		<b>439</b>
<1 year	14.25%	63	20.27%	89
1-5 years	40.72%	180	41.69%	183
6-10 years	22.17%	98	18.91%	83
>10 years	22.85%	101	19.13%	84
<b>Work-related stress level</b>		<b>460</b>		<b>465</b>
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24

3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66
7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

Note

<sup>a</sup> different income classes in Switzerland and Germany/ Austria

Spearman correlation between professional experience and length of time in the current employment was  $r=0.490$  ( $p<0.001$ ).

Associations between endometriosis and work outcomes are presented in Table IIIb.

In the adjusted analysis, all predictor variables plus nationality, occupation and number of pregnancies were included simultaneously as covariates.

**Table IIIb: Associations between endometriosis and parameters of professional life including the proportion of variance explained by the disease**

Predictor	Reference category	Unadjusted OR (95% CI)	Adjusted OR (95% CI) <sup>b</sup>	Pseudo R <sup>2</sup>
Own income	0-3000 CHF	0.85 (0.58-1.24); $p=0.396$	1.01 (0.56-1.83); $p=0.975$	0.011
	3001-6000 CHF	1.26 (0.87-1.84); $p=0.227$	1.23 (0.78-1.96); $p=0.376$	
	>6000 CHF	Ref.	Ref.	
Desired profession	No	2.14 (1.53-2.99); $p<0.001^{\#}$	1.84 (1.15-2.94); $p=0.011$	0.029
	Partially	1.43 (1.04-1.97); $p=0.026$	1.51 (1.02-2.23); $p=0.038$	
	Yes	Ref.	Ref.	
Degree of health-related limitations in career choice	Strongly	4.42 (2.50-7.83); $p<0.001^{\#}$	4.79 (2.30-9.96); $p<0.001$	0.063
	Moderately	2.32 (1.59-3.40); $p<0.001^{\#}$	2.61 (1.64-4.15); $p<0.001$	
	Not at all	Ref.	Ref.	
Estimation of adequacy of job qualification	Lower	1.25 (0.89-1.77); $p=0.195$	0.86 (0.55-1.35); $p=0.515$	0.012
	Higher	1.82 (1.18-2.80); $p=0.007^{\#}$	1.44 (0.87-2.41); $p=0.160$	
	Adequate	Ref.	Ref.	
Professional experience	<5 years	0.48 (0.35-0.66); $p<0.001^{\#}$	0.44 (0.28-0.71); $p=0.001$	0.033
	5-10 years	1.03 (0.75-1.41); $p=0.875$	1.02 (0.67-1.57); $p=0.916$	
	>10 years	Ref.	Ref.	
Duration of current employment	<1 year	0.59 (0.38-0.91); $p=0.017$	0.84 (0.47-1.50); $p=0.552$	0.011
	1-5 years	0.82 (0.57-1.17); $p=0.268$	1.14 (0.71-1.84); $p=0.584$	
	6-10 years	0.98 (0.65-1.48); $p=0.931$	0.99 (0.60-1.65); $p=0.975$	
	>10 years	Ref.	Ref.	
Work-related stress level	1 point increase <sup>a</sup>	1.09 (1.03-1.15); $p=0.002^{\#}$	1.04 (0.97-1.12); $p=0.230$	0.014

Note

<sup>#</sup> Statistically significant at Bonferroni corrected  $\alpha=0.007$

<sup>a</sup> On a scale from 0 (not stress at all) to 10 (extremely severe stress)

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3 356 <sup>b</sup> Adjusted for all other predictor variables plus nationality, occupation, and number of pregnancies

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6 358 Results of the main outcome measures “health influences on career choice”, “desired  
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8 359 profession” and “professional experience” are highly significant; even if the proportion  
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10 360 of variance explained by the last two factors was rather small. Excluding participants  
11  
12 361 who are members of self-help groups did not alter the results.  
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17 363 The intensity of reported health-related limitations in career choice was independent  
18  
19 364 from rASRM-stage ( $\chi^2$ , 16.51, df=12, p=0.169), but associated with the occurrence of  
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21 365 chronic pain ( $\chi^2$ , 34.39, df=4, p<0.001) as well as with the frequency of pain ( $\chi^2$ ,  
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23 366 25.62, df=8, p=0.001).  
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28 368 Chronic pain was also associated with higher levels of stress at work, even if the  
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30 369 mean difference was small (6.61 vs 5.47, SD=2.39/2.49, p<0.001).  
31

32  
33 370 Intraoperative findings of spread of endometriosis lesions showed varying  
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35 371 associations with health-related limitations in career choice: having endometriosis  
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37 372 lesions at the pelvic wall ( $\chi^2$ , 11.14, df=4, p=0.025) or in the sacrouterine ligaments  
38  
39 373 ( $\chi^2$ , 13.51, df=4, p=0.009) was significantly associated with greater limitations in  
40  
41 374 career choice, while such an outcome could not be found for localization in the  
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43 375 vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of stress  
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45 376 at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50,  
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47 377 SD=2.46/2.48, p=0.001), but not with other intraoperative findings.  
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### 51 379 **Work impairment and compensatory mechanisms**

52  
53 380 Asked about the amount of sick leave due to endometriosis during the last month,  
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55 381 78.1% of the women of the case group reported no sick leave, 8.5% reported one to  
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382 three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and  
383 8.1% reported two to four weeks.

384 Altogether, 13.1% of endometriosis patients used one week or more of overtime or  
385 vacation during the last year when they felt too sick to work due to symptoms of  
386 endometriosis. Furthermore, 75.5% of women with endometriosis reported to have  
387 gone to work during the previous month in spite of severe pain. Asked about the  
388 previous year, 89.2% of women with endometriosis affirmed to have worked despite  
389 pain. Out of the women diagnosed with endometriosis, 89.8% noted a loss of work  
390 productivity due to endometriosis, with 65.1% reporting strong or very strong  
391 limitations when symptoms were severe. On days with minimal endometriosis  
392 symptoms, 75.3% still felt some degree of loss of productivity.

393 A minority of women with endometriosis reported working part time (10.3%) or giving  
394 up work entirely (5.8%) due to their disease (n=445).

### 396 **Association of endometriosis-related symptoms with sick leave and** 397 **productivity loss**

398 We then examined whether different endometriosis symptoms were related to  
399 absenteeism and impaired work productivity (Table IV).

401 **Table IV: Association of endometriosis-related symptoms to sick leave and**  
402 **productivity loss in the last month**

Predictor		Sick leave <sup>a</sup>		Productivity loss <sup>b</sup>	
		OR (95% CI)	R <sup>2</sup>	OR (95% CI)	R <sup>2</sup>
Chronic pain	Yes	3.52 (2.02; 6.13); p<0.001 <sup>#</sup>	0.072	3.08 (2.11; 4.50); p<0.001 <sup>#</sup>	0.087
	No	Ref.		Ref.	
Frequency of pain	Daily	2.82 (1.47; 5.39); p=0.002 <sup>#</sup>	0.053	1.81 (1.05; 3.12); p=0.032	0.040
	>1 per week	1.40 (0.66; 2.97); p=0.377		0.76 (0.42; 1.38); p=0.369	
	≤1 per week	Ref.		Ref.	
Frequency of fatigue	Frequently	3.50 (1.76; 6.94); p<0.001 <sup>#</sup>	0.073	3.99 (2.49; 6.39); p<0.001 <sup>#</sup>	0.107
	Sometimes	1.15 (0.50; 2.64); p=0.748		1.44 (0.86; 2.41); p=0.168	

	Rarely	Ref.		Ref.	
Psychological symptoms <sup>c</sup>	Yes	3.03 (1.77; 5.18); p<0.001 <sup>#</sup>	0.061	2.90 (1.98; 4.23); p<0.001 <sup>#</sup>	0.082
	No	Ref.		Ref.	

404 Note

405 <sup>#</sup> Statistically significant at Bonferroni corrected  $\alpha=0.01$

406 <sup>a</sup> Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days

407 <sup>b</sup> Refers to current maximal impairments; Scale: 1="not at all/little", 2="moderately/strong", 3="very strong"

408 <sup>c</sup> depressive mood/anxiety/reduced resilience of more than three months

409

410 Corrected for multiple testing, all four predictor variables were significantly associated  
 411 with sick leave during the previous four weeks. The occurrence of chronic pain as  
 412 well as the frequency of fatigue and concomitant psychological symptoms were  
 413 associated with significantly higher degrees of perceived productivity loss. Including  
 414 age and time since diagnosis as potential confounders did not alter the results.  
 415 Likewise, the factor of different localisations of endometriosis was not associated with  
 416 sick leave or productivity loss (all  $p>0.05$ ).

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418

## 419 Discussion

420

421 Endometriosis is associated with impairment of professional activity: women  
 422 diagnosed with endometriosis showed a lower likelihood of working in their desired  
 423 profession and stronger health-related limitations in their career decisions. In  
 424 contrast, they had professional experience of longer durations. All of these main  
 425 outcomes were not reported previously and open new insights into the professional  
 426 life of women with endometriosis. Endometriosis-associated symptoms and symptom  
 427 characteristics were moderately related to sick leave and loss of productivity, but in

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3 428 contrast to our expectations, endometriosis was not associated with increased work-  
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5 429 related stress levels.

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9 431 In contrast to remarkable differences regarding parameters of working life, education  
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11 432 level did not differ significantly between case and control groups (Table I); this is a  
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13 433 result that has been described previously.<sup>13</sup> Other studies, however, reported serious  
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15 434 effects of endometriosis on education level, especially on tertiary formation.<sup>8 20</sup> These  
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17 435 contrasting findings might result from differences in study groups, e.g. with regard to  
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19 436 the onset of disease symptoms in relation to education, professional training and  
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21 437 professional activity. Many studies report an average age of first symptoms between  
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23 438 20 and 29 years,<sup>6 31-33</sup>. In our study the average age of diagnosis is 33.7 years. Even  
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25 439 if many of these women report the onset of endometriosis-related symptoms several  
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27 440 years before diagnosis, it is still an age at which most women have completed  
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29 441 professional training. As a consequence, the women investigated in such cohorts will  
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31 442 not experience a negative impact of endometriosis on their education, because they  
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33 443 were still symptom-free at this age. Other authors reported an earlier onset of  
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35 444 disease symptoms,<sup>34</sup> and emphasized that endometriosis in adolescent girls was an  
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37 445 underestimated problem.<sup>33 35 36</sup> Consequently, those women, which suffer from  
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39 446 endometriosis symptoms already at a young age, might feel limitations due to the  
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41 447 disease also early in life, namely already during education.

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44 448 On the other hand, there might be a higher tolerance for sick leave and impaired  
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46 449 energy levels in a school or university setting compared to in paid employment.

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51 451 Health issues are important criteria in career choice, and women diagnosed with  
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53 452 endometriosis do work less often in their desired profession. However, women with  
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55 453 endometriosis reported a greater length of experience in the current profession  
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3 454 (Table IIIb). Professional experience and the length of time a woman is working with  
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5 455 the current employer are highly correlated. These results can be interpreted  
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7 456 positively in the sense that women with endometriosis were successful in carefully  
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9 457 choosing a long-term profession. On the other hand, women might feel less able to  
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11 458 change the professional field and stuck in an undesired profession because of  
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13 459 endometriosis.

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20 462 Several authors reported elevated levels of general<sup>37 38</sup> as well as emotional<sup>21</sup>  
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22 463 distress in women diagnosed with endometriosis. This first study on work-specific  
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24 464 stress in endometriosis affected women produced results in contrast to our  
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26 465 expectations. Even though women reported that they sometimes went to work  
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28 466 despite endometriosis-associated pain, women with endometriosis did not  
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30 467 experience higher work-related stress levels than the control women; but within the  
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32 468 group of women with endometriosis, those with chronic pain reported significantly  
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34 469 higher work-related stress than those without pain. We investigated women whose  
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36 470 initial diagnosis was up to 20 years ago; these women may have meanwhile found an  
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38 471 occupation meeting their needs, and superiors and colleagues may have adapted to  
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40 472 their sometimes reduced availability for work. Also, the fact that work can be a source  
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42 473 of distraction and of self-esteem for individuals suffering from a chronic disease<sup>39</sup>  
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44 474 may offset stressful situations.

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48 475 According to our results and those of others,<sup>34</sup> women affected by endometriosis  
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50 476 compensate for their health-related restrictions at work by using overtime or vacation  
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52 477 for absences as well as by saving energy for work through reduction of leisure time  
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54 478 activities.

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3 480 Despite these personal efforts to adapt to an adverse situation, productivity loss<sup>9 15</sup>  
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5 481 and sick leave<sup>9 10</sup> are relevant issues for many women diagnosed with endometriosis.  
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7 482 Average loss of work time per week (absenteeism) due to endometriosis is reported  
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9 483 to be between 4.4 and 7.4 hours.<sup>9 10</sup> In our study, chronic pain, the frequency of pain,  
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11 484 fatigue, and psychological symptoms, such as self-reported depression and anxiety,  
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13 485 were significantly - but with modest effect sizes - related to taking more sick leave  
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15 486 (Table IV). Productivity loss at work due to endometriosis-related symptoms was  
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17 487 described to be high or very high – depending on the current severity of symptoms –  
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19 488 by up to 65% of women in the present study. Struggles to fulfil normal demands of  
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21 489 work might be exacerbated by the side effects of treatment, for example by dizziness  
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23 490 from strong pain killers.<sup>18 19</sup> Although, the majority of women affected with  
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25 491 endometriosis seemed to be able to compensate for disease-related difficulties at  
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27 492 work and to realize successful long-term professional activity, 16.2% of the women  
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29 493 nevertheless reduced or even gave up work entirely due to endometriosis-related  
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31 494 symptoms; this is a situation that has been observed also by others.<sup>13</sup> Furthermore, a  
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33 495 very similar percentage of women with endometriosis and control women worked part  
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35 496 time, even though women diagnosed with endometriosis remained childless more  
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37 497 often. Such decisions may result from feeling pressured to reduce or quit work when  
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39 498 employers know about a chronic disease such as endometriosis.<sup>8 20</sup> More flexible  
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41 499 work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted  
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43 500 physical demands, the possibility to lie down, and the existence of bathrooms nearby  
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45 501 are seen to be helpful resources for successful professional performance in women  
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47 502 with endometriosis.<sup>19 20</sup>  
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55 504 As for the relationship between rASRM stage and endometriosis-associated  
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57 505 symptoms,<sup>1 3</sup> none of the parameters evaluating professional activity showed any  
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3 506 significant association with rARSM stage. Testing the association between different  
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5 507 intraoperative findings of endometriotic lesions and work outcomes showed  
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7 508 inconsistent results. In contrast, most outcome measures were related to the  
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9 509 occurrence and frequency of chronic pain; this result is supported by other studies on  
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11 510 endometriosis,<sup>10 15</sup> as well as on other chronic pain conditions such as migraine or  
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13 511 fibromyalgia.<sup>40 41</sup> Even if the effect size of pain on work in this study is limited,  
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15 512 findings support the relevance of pain management for satisfactory work  
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17 513 performance. Fatigue, either as a symptom of endometriosis or as a frequent  
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19 514 comorbidity,<sup>42</sup> interfered with professional activity in this as well as in other studies.<sup>1 9</sup>  
20  
21 515 In summary, it may be that women with endometriosis strive for normality at their  
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23 516 work place, even if it is associated with reduced professional flexibility or with giving  
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25 517 up the desire for another profession.  
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31 519 This study presents one of the largest samples investigating the association between  
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33 520 endometriosis and professional life and it is one of the very few studies providing a  
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35 521 control group. Study participants were recruited in university hospitals, in district  
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37 522 hospitals and in doctors' practices in order to collect a representative sample. The  
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39 523 pair matching with regard to age and ethnic background reduced the confounding  
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41 524 effect of these factors. A meticulous review of all surgical records by the same  
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43 525 investigator (AKS) ensured high data quality with regard to diagnosis and  
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45 526 classification of endometriosis. The response rate of 64.1% in the case group is in  
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47 527 the upper level of comparable studies,<sup>8 9</sup> whereas the response rate of 35.8% in the  
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49 528 control group is comparatively low. We cannot exclude that women with a particularly  
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51 529 high work load refrained from study participation; however, such an effect is equally  
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53 530 relevant in women diagnosed with endometriosis and in controls. The higher  
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3 531 response rate in women with endometriosis supports the fact that such an  
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5 532 association does not represent a particular problem for members in this group.

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7 533 Given the methodology of a self-reported questionnaire answered retrospectively,  
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9 534 distortions in the sense of falsely or overly attributing dissatisfaction on the job to  
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11 535 endometriosis cannot be excluded. By addressing questions on professional activity  
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13 536 either current or in the period just prior to study participation, we tried to reduce recall  
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15 537 bias. As we included only patients with a confirmed diagnosis of endometriosis, and  
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17 538 as such a confirmation can be provided only by surgery, there may be referral bias.  
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19 539 For example, affected but asymptomatic women and symptomatic women who do  
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21 540 not have access to or refused surgery might have been excluded. In contrast,  
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23 541 asymptomatic women with endometriosis might have been included in the control  
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25 542 group which would result in underestimation of results. As we have no differentiated  
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27 543 information on symptoms resulting from diseases other than endometriosis, in both  
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29 544 groups further confounders might be present; this would also result in  
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31 545 underestimation of our findings. A comparison group for the questions of sick leave  
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33 546 and productivity loss at work would have been beneficial. However, analysis of  
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35 547 impact of different endometriosis-related symptoms on these two outcomes allowed  
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37 548 for indirect conclusions on the association between endometriosis and reduced  
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39 549 working ability, as well as basic data to design future studies.  
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## 47 48 552 **Conclusion**

49  
50 553 Even if most measured effect sizes of associations between endometriosis and  
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52 554 individual parameters of working life were small, the study confirms a burdensome  
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54 555 influence of the disease on the working life of women affected by endometriosis.  
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56 556 Therefore, medical and psychological support should address such issues in order to  
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3 557 support women in adjusting their professional choices and professional development  
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5 558 to individual endometriosis-related conditions. Furthermore, for professionals in  
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7 559 occupational medicine, insurances, politics etc. it might be useful to know about  
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9 560 endometriosis-related challenges and limitations in professional activity.

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29  
30 570 manuscript.

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### 37 38 39 574 **Authors roles**

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43 576 drafting and finalization of the manuscript

44  
45 577 MPH: statistical analysis, interpretation of data, finalization of manuscript

46  
47 578 AKS: investigator, collection of data on site in Winterthur, Switzerland, verification of  
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49 579 surgical reports, finalization of the manuscript

50  
51 580 KG: concept of study, collection of data on site in Zurich, management databank,

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53 581 finalization of the manuscript

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2  
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7 584 MW: investigator, collection of data on site in Aachen, Germany, and in Graz,  
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9 585 Austria, finalization of the manuscript

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11 586 FH: investigator, collection of data on site in St. Gallen, Switzerland, finalization of  
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17 589 manuscript

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23 592 FM: concept of study, investigator on site in Solothurn, Switzerland, finalization of  
24  
25 593 manuscript

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27 594 BI: concept of study, investigator on site in Zurich, Switzerland, interpretation of data,  
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29 595 finalization of manuscript

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31 596 PI: concept of study, investigator and data collection in Zurich, Switzerland,  
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33 597 finalization of the manuscript

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35 598 BL: principal investigator, concept and conduct of study, investigator on site in Zurich,  
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37 599 Switzerland, collection and analysis of data, preparation and finalization of

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39 600 manuscript

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43 602 **References**

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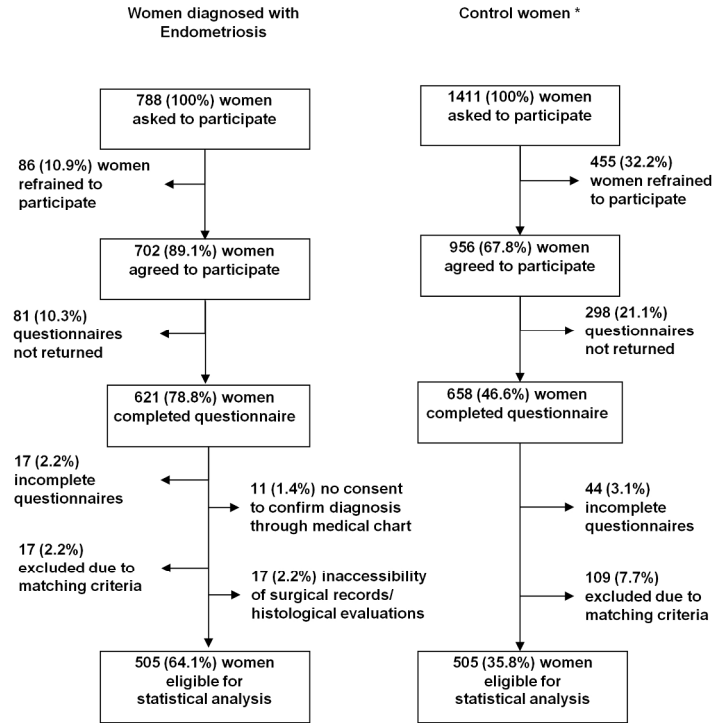
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708 **Figure Legend**

709 Fig 1.: Recruitment of study participants

For peer review only

Flow chart I. Recruitment of study participants



\* women presenting for routine gynaecological care or benign gynaecological surgery

190x274mm (284 x 284 DPI)

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8/9
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	7

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Does endometriosis affect professional life? – a matched case-control study

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<b>Primary Subject Heading</b>:	Obstetrics and gynaecology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Endometriosis, work, professional life, pain, stress, career choice

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Manuscripts

# 1 Does endometriosis affect professional life? – 2 a matched case-control study

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2  
3 35 **Abstract**  
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5 36 **Objectives:** Endometriosis is a gynaecological disease most commonly causing  
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8 37 severe and chronic pelvic pain as well as an impaired quality of life. The aim of this  
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11 38 study was to investigate if and how endometriosis affects choices regarding  
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13 39 professional life as well as the quality of daily working life.  
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16 40 **Design, setting, and participants:** In the context of a multicentre case-control  
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19 41 study, we collected data from 505 women with surgically/histologically confirmed  
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21 42 diagnosis of endometriosis and 505 matched controls. Study participants were  
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23 43 recruited prospectively in hospitals and doctors' practices in Switzerland, Germany,  
24  
25 44 and Austria. Using a detailed questionnaire, the study investigated work-life and  
26  
27 45 career choices of study participants.  
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30 46 **Main outcome measures:** Associations between endometriosis/ disease symptoms  
31  
32 47 and limitations in career development as well as ability to work.  
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34 48 **Results:** Women with endometriosis were less often able to work in their desired  
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36  
37 49 profession than women from the control group (adjusted OR=1.84, 95%-CI: 1.15-  
38  
39 50 2.94,  $R^2=0.029$ ,  $p=0.001$  and they had to take health-related limitations into  
40  
41 51 consideration in their career decisions to a significantly higher degree than women in  
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43 52 the control group (aOR=4.79, 95%-CI: 2.30-9.96,  $R^2=0.063$ ,  $p<0.001$ ). Among  
44  
45 53 women with endometriosis, chronic pain was significantly associated with increased  
46  
47 54 sick leave (OR=3.52, 95%-CI: 2.02-6.13,  $R^2=0.072$ ,  $p<0.001$ ) as well as with loss of  
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49 55 productivity at work (OR=3.08, 95%-CI: 2.11-4.50,  $R^2=0.087$ ,  $p<0.001$ ).  
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53 56 **Conclusions:** Endometriosis is associated with impairment of professional life, in  
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56 57 particular with regard to career choices. Further research to develop strategies to  
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3 58 support endometriosis-affected women in realizing professional opportunities is  
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5 59 recommended.

### 60 **Strengths and limitations of this study**

61 This study presents one of the largest samples investigating the association between  
62 endometriosis and professional activity. It is one of the first studies in this field to  
63 provide a matched control group.

64 Recruitment of study participants in university hospitals, in district hospitals and in  
65 private doctors' practices ensured a representative sample.

66 Validation of diagnosis and stage of endometriosis by case reports provided high  
67 data quality.

68 Given the design of the study (using a self-reported questionnaire answered  
69 retrospectively), distortions in the sense of false or excessive attribution of  
70 professional dissatisfaction to endometriosis cannot be excluded.

71 As we did not investigate diseases or symptoms that may also have had an impact  
72 on professional life in the control group, results may be underestimated.

73

### 74 **Trial registration number**

75 Clin.trial.gov: Endo\_QOL NCT02511626

76

### 77 **Funding**

78 This research received no specific grant from any funding agency in the public,  
79 commercial, or not-for-profit sectors.

80

### 81 **Conflict of interest**

82 The authors do not have any conflicts of interest.

83



## 84 **Data sharing statement**

85 The data set is available on request from the corresponding author.

86

87 **Key words:** Endometriosis, work, professional life, stress, career choice

88

89

## 90 **Introduction**

91

92 Endometriosis is a gynaecological disease defined by the presence of endometrium-  
93 like tissue outside the uterine cavity.<sup>1</sup> The prevalence of the disease among women  
94 of reproductive age is estimated to be between 8 and 10%.<sup>2 3</sup> However, as reliable  
95 diagnosis of endometriosis can only be made by surgery and endometriosis can be  
96 asymptomatic, an unknown number of affected women might remain undiagnosed  
97 e.g. prevalence might be far higher.<sup>4</sup>

98

99 Women suffering from endometriosis experience most commonly one or more of the  
100 following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia,  
101 pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea,  
102 as well as reduced fertility and chronic fatigue.<sup>5 6 7</sup> Numerous and severe symptoms,  
103 the chronicity of the disease<sup>8</sup>, side effects of therapies<sup>9</sup> as well as diagnostic delays<sup>10</sup>  
104 <sup>11</sup> significantly affect women's overall quality of life, including professional  
105 performance, and place high demands on the treating physicians.<sup>12 13 14</sup> For most  
106 patients, available treatment options, such as analgesics, various hormonal  
107 therapies, and radical laparoscopy<sup>1</sup> are often not curative and are associated with  
108 significant side effects.<sup>12 15</sup>

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3 109 Consequently, disease symptoms, especially endometriosis-related pain and fatigue,  
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5 110 may disturb the development and realization of long-term goals such as a  
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7 111 professional career<sup>16</sup> and may make it difficult to meet the demands of a job. About  
8  
9 112 40% of women with endometriosis report impaired career growth due to  
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11 113 endometriosis,<sup>13</sup> and about 50% experience a decreased ability to work due to their  
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13 114 chronic disease.<sup>12 17</sup> Differentiated knowledge on the nature of such limitations and in  
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15 115 particular on how adjustments to professional life can be made to improve  
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17 116 professional performance is currently lacking.

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20 117 The quality of working life is a major aspect in quality of life overall,<sup>18</sup> which in turn is  
21  
22 118 the most important predictor of total cost of disease.<sup>19</sup> About 66% to 75% of the total  
23  
24 119 costs of endometriosis arise from reduced ability to work and not from direct costs of  
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26 120 treatment.<sup>19 20</sup> Being able to work in a desired occupation may not only have a strong  
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28 121 impact on a woman's financial situation and on the perception of and attitude toward  
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30 122 daily work, but can also be an important health factor. For example, unsatisfactory  
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32 123 work and limited possibilities for change are associated with increased levels of  
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34 124 headache, fatigue and depressed mood.<sup>21</sup>

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37 125 Frequent sick leave and reduced work productivity can put affected women under  
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39 126 observation by superiors and under greater pressure to deliver full performance.<sup>22 23</sup>

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41 127 The rather intimate and gender-specific nature of the most common endometriosis  
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43 128 symptoms tends to make affected women feel embarrassed.<sup>24</sup> Consequently, some  
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45 129 women may avoid discussing endometriosis-related problems with superiors and  
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47 130 colleagues, particularly if the superiors and colleagues are male.<sup>24 25</sup> Due to the  
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49 131 invisibility of their disease, women can be easily perceived as malingerers.<sup>24</sup>  
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51 132 Therefore, medical professionals need to know how the symptoms of endometriosis  
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53 133 can affect daily working life and professional development, notably because  
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55 134 endometriosis-affected women repeatedly underline their wish for comprehensive  
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3 135 information<sup>24 26 27</sup> and advice in managing their disease in daily life,<sup>26 27</sup> instead of  
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5 136 isolated treatment of endometriosis symptoms.<sup>24 26 27</sup> A better understanding of  
6  
7 137 endometriosis and its impacts on any aspect of life - including professional activity -  
8  
9 138 not only by medical professionals but also in society and politics would help affected  
10  
11 139 women and their families to reduce negative consequences of the disease. However,  
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13 140 research on quantitative and qualitative impairment of working life as the necessary  
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15 141 background for offering adequate support and interventions is scarce and relies  
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17 142 mainly on interview-based studies with small samples of affected women<sup>23 24</sup>; there is  
18  
19 143 only one other study that uses a control group.<sup>14</sup> In addition, work-related stress in  
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21 144 women diagnosed with endometriosis has not been investigated yet.

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24 145 Therefore, it was the aim of the present study to investigate parameters of working  
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26 146 life of a larger number of endometriosis-affected women, and compare findings with  
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28 147 those of a matched control group. We investigated (i) perceived health-related  
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30 148 limitations in career decisions; (ii) quality of the current work situation; and (iii) the  
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32 149 association between endometriosis-related disease symptoms and work  
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34 150 performance.

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## 38 39 40 152 **Material and Methods**

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### 44 45 154 **Study design**

46  
47 155 The study is designed as a multicentre case-control study. Main outcome measures  
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49 156 are health limitations in career choice as well as quality and stability of the current  
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51 157 work situation. Secondary outcome measures investigate the impact of different  
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53 158 symptoms as well as localisation of endometriosis on sick leave and loss of  
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3 159 productivity. The study has been conducted and reported applying the criteria of the  
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5 160 STROBE Statement.<sup>28</sup>  
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## 8 9 162 **Recruitment**

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11 163 Recruitment of study participants is shown in Figure I. To detect a 10% difference  
12  
13 164 between cases and controls with an alpha of 0.05, and a power of 0.8 a sample size  
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15 165 of 387 participants in each group is needed. With the inclusion of 505 participants in  
16  
17 166 both groups we consequently reached very high power, for example 99.1 for the  
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19 167 detection of differences in desired profession or 99.7 for health-related limitations in  
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21 168 career choice. Study participants were recruited prospectively for a research project  
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23 169 on quality of life including professional activity in endometriosis-affected women  
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25 170 compared to control women.<sup>7 9 29 30 31</sup> Recruitment took place between January 2010  
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27 171 and December 2015 at the following hospitals and associated doctors' offices in  
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29 172 Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli  
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31 173 Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen,  
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33 174 Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes Humboldt  
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35 175 Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital Aachen,  
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37 176 and the University Hospital Graz. In doctors' offices one or several gynecologists  
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39 177 work together in a medical unit; district hospitals offer tertiary care associated with a  
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41 178 university.  
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45 179 Healthcare professionals carried out the recruitment of all study participants via direct  
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47 180 approach. The study was explained to the respondents and information about the  
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49 181 voluntary nature of participation as well as anonymity of data in reports and  
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51 182 publications was provided. Each participant received a detailed written description of  
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53 183 the study and signed informed consent. Participants were given all documents and a  
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55 184 return envelope.  
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3 185 Inclusion criteria: All study participants had to be between 18 and 50 years old. For  
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5 186 the case group, women with surgically and histologically diagnosed endometriosis  
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7 187 were included irrespective of stage, location of lesions, and severity and profile of  
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9 188 symptoms. Only data sets with at least 80% of answers for main and secondary  
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11 189 outcome measures were included.

13 190 Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic,  
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15 191 mental or psychological impairments that might affect their ability to understand and  
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17 192 to complete the questionnaire.

19 193 The most frequent reasons reported for not participating were lack of time and the  
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21 194 intimate nature of some of the questions. To maximize the return rate, women were  
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23 195 reminded to complete and return the questionnaire after one month and after three  
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25 196 months.

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28 197 A smaller segment of the case group (N=74, 66 of which could be included in the  
29  
30 198 final analysis (13.1% of total case group)) was recruited through different self-help  
31  
32 199 groups for endometriosis patients (in Germany only). Education levels and family  
33  
34 200 incomes in this cohort are similar to those in the main group. However, the women in  
35  
36 201 this cohort were significantly older than those in the hospital group ( $42.45 \pm 6.03$   
37  
38 202 versus  $37.02 \pm 7.21$  years,  $p < 0.001$ ), showed a longer time since primary diagnosis  
39  
40 203 ( $82.11 \pm 8.36$  versus  $37.20 \pm 44.00$  months,  $p < 0.001$ ), and presented at the time of the  
41  
42 204 study a significantly higher stage of disease ( $p = 0.013$ ).

43  
44  
45 205 Control women were recruited during regular annual or biennial gynaecological  
46  
47 206 consultations at hospitals' out-patient clinics or in private offices, as part of standard  
48  
49 207 healthcare in the three countries where recruitment took place. In addition, women  
50  
51 208 during hospital stays because of temporary mild benign gynaecological problems  
52  
53 209 other than endometriosis were invited to participate in the study. Each control woman  
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3 210 was matched to a woman diagnosed with endometriosis for age ( $\pm 3$  years) and  
4  
5 211 ethnic background, i.e. Caucasian or not (pair matching).  
6

7 212

8  
9 213 **Questionnaire**

10  
11 214 The structured self-administered questionnaire for the total study on quality of life  
12  
13 215 contained 390 questions for all participants and 90 additional specific questions for  
14  
15 216 women diagnosed with endometriosis. It is structured in different chapters, one of  
16  
17 217 which is professional life. Further chapters covered questions regarding life style;  
18  
19 218 general wellbeing; general, gynaecological, and medical history; childhood  
20  
21 219 experiences; sexuality and partnership. Women diagnosed with endometriosis were  
22  
23 220 additionally asked to provide detailed information on the diagnosis and treatment of  
24  
25 221 endometriosis, symptoms of endometriosis, sick leave, and productivity loss due  
26  
27 222 specifically to endometriosis. Wherever possible we used internationally validated  
28  
29 223 questionnaires. Modified versions of the Brief Pain Inventory<sup>32</sup> and the Pain Disability  
30  
31 224 Index<sup>33 34</sup> served to evaluate pain. For several questions about professional life as for  
32  
33 225 occupation, sick leave and productivity loss, we used similar reporting methods the  
34  
35 226 WPAI<sup>35</sup> suggests, but extended the time period of reporting from only seven days in  
36  
37 227 the WPAI to four weeks and one year. Level of education was measured with defined  
38  
39 228 categories following the recommendation to use meaningful benchmarks of  
40  
41 229 educational attainment rather than a continuous scale in years.<sup>36</sup> In order to capture  
42  
43 230 the professional situation of women diagnosed with endometriosis as close to reality  
44  
45 231 as possible a interdisciplinary research team including specialists for minimally  
46  
47 232 invasive endometriosis-surgery, for gynaecological endocrinology and for gynaeco-  
48  
49 233 psychosomatic medicine added their clinical experience and evaluated systematically  
50  
51 234 what they had learned from individual patients. On this background specific questions  
52  
53 235 like on working despite pain or on using overtime or holidays to compensate for sick  
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3 236 leave were added. The first version of our questions on professional activity was than  
4  
5 237 revised by the governing body of the German self-help groups in order to map the  
6  
7 238 questions to the situations reported by women with endometriosis and to avoid using  
8  
9 239 questions, which do not correctly depict the specific situation in the context of  
10  
11 240 endometriosis.

12  
13 241 The analysis presented in this paper was based on answers to the following  
14  
15 242 questions asked to the case as well as to the control group: nationality (German,  
16  
17 243 Swiss, Austrian, other [with the possibility of entering nationality]), age (years),  
18  
19 244 marital status (married/cohabiting/single), highest achieved education level (lower  
20  
21 245 school education, high school education, apprenticeship, university degree, no formal  
22  
23 246 education, other), current own monthly net income (six choices for responses ranging  
24  
25 247 from none to >2500 Euros for participants in Germany and Austria and from none to  
26  
27 248 >6000 Swiss francs for participants in Switzerland), numbers of pregnancies of more  
28  
29 249 than 24 weeks of gestation. Women were asked to report their levels of current  
30  
31 250 employment (full-time/part-time/full-time housekeeping/student/registered as  
32  
33 251 unemployed) and whether they currently worked in their desired profession (yes/no).  
34  
35 252 This question does not ask about the current place of employment but on the  
36  
37 253 profession itself, e.g. for a woman who always wanted to be a teacher, is she now  
38  
39 254 able to work as a teacher? They were asked how they perceived their level of  
40  
41 255 qualification for the currently held job (overqualified, about right, under-qualified),  
42  
43 256 length of professional experience (<5 years, 6-10 years, and >10 years), years  
44  
45 257 working with the current employer (<1 year, 1-5 years, 6-10 years, >10 years), the  
46  
47 258 subjectively perceived influence of health-related limitations on career choice (not at  
48  
49 259 all, little, medium, strongly, exclusively) and perceived current level of stress on the  
50  
51 260 job (scale from 0=none to 10=very strong).  
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3 261 The analysis presented in this paper further used the following questions asked only  
4  
5 262 to women diagnosed with endometriosis: Amount of time since first symptoms of  
6  
7 263 endometriosis were noticed (<1 year ago/1 year ago/2-5 years ago/6-10 years  
8  
9 264 ago/>10 years ago), date of initial diagnosis of endometriosis (month and year),  
10  
11 265 number of surgeries related to endometriosis (1/2/3/4/5/6 or more), chronic pain  
12  
13 266 (yes/no), duration of pain (<1 year/1-3 years/4-5 years/6-10 years/11-20 years/>20  
14  
15 267 years), frequency of pain (a few times per year/a few times per month/several times  
16  
17 268 per week/once a day/several times a day/permanently), cyclic pain (yes/no),  
18  
19 269 psychological symptoms lasting more than three months estimated by the study  
20  
21 270 participant to be related to endometriosis, such as depressive mood/anxiety/reduced  
22  
23 271 resilience (yes/no), days worked despite pain during the last month (never/1-3  
24  
25 272 days/4-7 days/1-2 weeks/2-4 weeks), frequency of fatigue or exhaustion due to  
26  
27 273 endometriosis (never/rarely/sometimes/often/very often), sick leave due to symptoms  
28  
29 274 of endometriosis (not specified) during the last month (never/1-3 days/4-7 days/1-2  
30  
31 275 weeks/2-4 weeks), sick leave due to symptoms of endometriosis in the last year  
32  
33 276 (never/1-7 days/1-2 weeks/2-4 weeks/4-8 weeks/8-12 weeks/>12 weeks), estimated  
34  
35 277 loss of productivity due to endometriosis when symptoms are at their maximum or at  
36  
37 278 their minimum respectively (no loss/a little/somewhat/high), reduction of work time  
38  
39 279 due to endometriosis (no reduction/reduction of 25%/50%/75%), and giving up  
40  
41 280 employment entirely due to endometriosis (yes/no). (Chronic pelvic pain included  
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43 281 cyclic as well as non-cyclic pelvic pain.)  
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45  
46  
47

48 282 The study was registered at [clinicaltrials.gov](http://clinicaltrials.gov) (NCT 02511626), where further details  
49  
50 283 on the complete questionnaire are available.  
51

52 284

## 53 54 55 285 **Verification of diagnosis and stage of endometriosis**



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3 286 To verify diagnosis and obtain information about localization of endometriosis  
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5 287 lesions, surgical records as well as the histological diagnosis of each patient and  
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7 288 each intervention were collected from medical charts. Stage was classified according  
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9 289 to the revised Classification of the American Society for Reproductive Medicine  
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11 290 (rASRM).<sup>37</sup>

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### 15 292 **Ethical approval**

16  
17  
18 293 The study was approved by the Swiss ethics commission as well as by the ethics  
19  
20 294 boards of participating hospitals. This study followed the guidelines of the World  
21  
22 295 Medical Association Declaration of Helsinki 1964, updated in October 2013.

23  
24  
25 296

### 26 297 **Patient and Public Involvement statement**

27  
28 298 Questions for this study were selected in cooperation with endometriosis self-help  
29  
30 299 groups. Other than in the self-help groups patients were not involved in the  
31  
32 300 recruitment and conduct of the study. All interested study participants receive the  
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34 301 publications resulting from the study. Publications are also sent to the governing  
35  
36 302 body of the self-help groups.

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### 40 304 **Statistical analysis**

41  
42 305 Differences in sample characteristics between study groups were computed with  
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44 306 either independent sample t-tests for continuous variables or Pearson  $\chi^2$ -tests for  
45  
46 307 categorical variables. To test associations between study groups and characteristics  
47  
48 308 of professional life, we conducted a series of binomial logistic regression. The study  
49  
50 309 group, i.e. women with endometriosis as opposed to controls without endometriosis,  
51  
52 310 was included as the dependent variable. To test association between symptoms of  
53  
54 311 endometriosis and work outcomes in women with endometriosis, we conducted a

series of ordinal logistic regression, entering work outcomes as the dependent variable. The proportion of variance explained based on the study group was indicated by Nagelkerke's pseudo  $R^2$ . Sample characteristics that differed significantly between study groups were statistically adjusted for by including them simultaneously as covariates. Initially,  $\alpha$  was set at 5%, but we applied Bonferroni correction to adjust the significance level  $\alpha$  for multiple testing. All analyses were conducted with SPSS version 24 for Windows.

## Results

### Characteristics of study groups and possible confounders

A comparison of socio-epidemiological parameters between women with endometriosis and control women is presented in Table I. Significant variables, eg nationality, pregnancies, and paid employment, were included as covariates in subsequent analyses on case-control effects.

**Table I: Descriptive statistics and group comparisons**

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	$p=0.344^a$
Nationality	Swiss German Others	N=211 (42.2%) N=244 (48.8%) N=45 (9.0%)	N=285 (57.3%) N=161 (32.4%) N=51 (10.3%)	$p<0.001^b$
Marital status	Married/ Cohabiting Single	N=420 (83.3%) N=84 (16.7%)	N=397 (79.4%) N=103 (20.6%)	$p=0.109^b$
Pregnancies >24 weeks	0 1 $\geq 2$	N=331 (70.6%) N=83 (17.7%) N=55 (11.7%)	N=245 (50.9%) N=80 (16.6%) N=156 (32.4%)	$p<0.001^b$
Education level <sup>c</sup>	Low Medium High	N=71 (14.4%) N=245 (49.6%) N=178 (36.0%)	N=74 (14.7%) N=249 (49.4%) N=181 (35.9%)	$p=0.990^b$
Paid occupation	Full-time Part-time None	N=248 (49.8%) N=176 (35.3%) N=74 (14.9%)	N=206 (41.8%) N=186 (37.7%) N=101 (20.5%)	$p=0.016^b$

Occupation among mothers <sup>d</sup> only	Full-time	N=30 (22.1%)	N=57 (23.9%)	p=0.120 <sup>b</sup>
	Part-time	N=68 (50.0%)	N=136 (57.1%)	
	None	N=38 (27.9%)	N=45 (18.9%)	

329 Note

330 <sup>a</sup> Independent samples t-test

331 <sup>b</sup> Pearson  $\chi^2$ -test

332 <sup>c</sup> Scale: Low="no formal education/lower school education", Medium="higher school education/apprenticeship",  
333 High="university degree"

334 <sup>d</sup> women with at least one pregnancy >24 weeks

335

336 Disease characteristics of the endometriosis group are shown in Table II.

337 **Table II: Disease characteristics in women diagnosed with endometriosis**

Criteria		Endometriosis Group %	N
<b>Time since occurrence of first symptoms (N=474)</b>	<1 year	5.49%	26
	1 year	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	>10 years	42.19%	200
<b>rASRM-stage of endometriosis (N=502)</b>	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
<b>Number of endometriosis-related surgical interventions (N=505)</b>	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information <sup>a</sup>	7.33%	37
	Mean±SD	1.79±1.27	
<b>Douglas obliteration (N=503)</b>	Yes	26.6%	134
	No	73.4%	369
<b>Involvement of sacrouterine ligaments (N=503)</b>	Yes	61.4%	309
	No	38.6%	194
<b>Involvement of Douglas (N=503)</b>	Yes	72.0%	362
	No	28.0%	141
<b>Intra-abdominal adhesions (N=504)</b>	Yes	74.8%	377
	No	25.2%	127
<b>Involvement of pelvic wall (N=503)</b>	Yes	74.8%	377
	No	25.2%	127
<b>Involvement of vaginal fornix or septum rectovaginal (N=503)</b>	Yes	12.7%	64
	No	87.3%	439

<b>Endometrioma (N=502)</b>	Yes	49.0%	246
	No	51.0%	256
<b>Chronic pain (N=500)</b>	Yes	58.40%	292
	No	41.60%	208
<b>Duration of chronic pain</b>	<1 year	3.48%	10
	1-3 years	13.59%	39
	4-5 years	17.07%	49
	6-10 years	23.34%	67
	11-20 years	29.27%	84
	>20 years	13.24%	38
<b>Frequency of pain</b>	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
<b>Frequency of endometriosis-related fatigue/ exhaustion</b>	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Often	28.14%	141
	Very often	22.55%	113
<b>Psychological Symptoms due to endometriosis<sup>b</sup></b>	Yes	57.24%	261
	No	42.76%	195

Note

<sup>a</sup> question not answered but diagnosis of endometriosis confirmed with at least one surgical record

<sup>b</sup> depressive mood/anxiety/reduced resilience of more than three months

### Parameters of working life

Parameters of professional activity in women diagnosed with endometriosis and control women are presented in Table IIIa.

**Table IIIa: Parameters of professional activity in the case and the control group**

Criteria	Endometriosis group	N	Control group	N
<b>Own net income per month</b>		<b>480</b>		<b>483</b>
No income	11.25%	54	15.76%	76
<3000 CHF (1000 EUR) <sup>a</sup>	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500 EUR) <sup>a</sup>	49.17%	236	40.37%	195
>6000 CHF (>2500 EUR) <sup>a</sup>	14.79%	71	15.32%	74
<b>Desired profession</b>		<b>488</b>		<b>482</b>
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
<b>Degree of health-related limitations in</b>		<b>486</b>		<b>466</b>

<b>career choice</b>				
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
<b>Estimation of adequacy of job qualification</b>		<b>459</b>		<b>453</b>
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
<b>Professional experience</b>		<b>487</b>		<b>474</b>
<5 years	18.89%	92	32.70%	155
5-10 years	25.87%	126	21.10%	100
>10 years	55.24%	269	46.20%	219
<b>Duration of current employment</b>		<b>442</b>		<b>439</b>
<1 year	14.25%	63	20.27%	89
1-5 years	40.72%	180	41.69%	183
6-10 years	22.17%	98	18.91%	83
>10 years	22.85%	101	19.13%	84
<b>Work-related stress level</b>		<b>460</b>		<b>465</b>
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24
3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66
7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

347 Note

348 <sup>a</sup> different income classes in Switzerland and Germany/ Austria

349 Spearman correlation between professional experience and length of time in the  
 350 current employment was  $r=0.490$  ( $p<0.001$ ).

351

352 Associations between endometriosis and work outcomes are presented in Table IIIb.

353 In the adjusted analysis, all predictor variables plus nationality, occupation and  
 354 number of pregnancies were included simultaneously as covariates.

355

356 **Table IIIb: Associations between endometriosis and parameters of pro-**  
 357 **fessional life including the proportion of variance explained by the disease**

Predictor	Reference category	Unadjusted OR (95% CI)	Adjusted OR (95% CI) <sup>b</sup>	Pseudo R <sup>2</sup>
Own income	0-3000 CHF	0.85 (0.58-1.24); $p=0.396$	1.01 (0.56-1.83); $p=0.975$	0.011

	3001-6000 CHF >6000 CHF	1.26 (0.87-1.84); p=0.227 Ref.	1.23 (0.78-1.96); p=0.376 Ref.	
Desired profession	No Partially Yes	2.14 (1.53-2.99); p<0.001 <sup>#</sup> 1.43 (1.04-1.97); p=0.026 Ref.	1.84 (1.15-2.94); p=0.011 1.51 (1.02-2.23); p=0.038 Ref.	0.029
Degree of health-related limitations in career choice	Strongly Moderately Not at all	4.42 (2.50-7.83); p<0.001 <sup>#</sup> 2.32 (1.59-3.40); p<0.001 <sup>#</sup> Ref.	4.79 (2.30-9.96); p<0.001 2.61 (1.64-4.15); p<0.001 Ref.	0.063
Estimation of adequacy of job qualification	Lower Higher Adequate	1.25 (0.89-1.77); p=0.195 1.82 (1.18-2.80); p=0.007 <sup>#</sup> Ref.	0.86 (0.55-1.35); p=0.515 1.44 (0.87-2.41); p=0.160 Ref.	0.012
Professional experience	<5 years 5-10 years >10 years	0.48 (0.35-0.66); p<0.001 <sup>#</sup> 1.03 (0.75-1.41); p=0.875 Ref.	0.44 (0.28-0.71); p=0.001 1.02 (0.67-1.57); p=0.916 Ref.	0.033
Duration of current employment	<1 year 1-5 years 6-10 years >10 years	0.59 (0.38-0.91); p=0.017 0.82 (0.57-1.17); p=0.268 0.98 (0.65-1.48); p=0.931 Ref.	0.84 (0.47-1.50); p=0.552 1.14 (0.71-1.84); p=0.584 0.99 (0.60-1.65); p=0.975 Ref.	0.011
Work-related stress level	1 point increase <sup>a</sup>	1.09 (1.03-1.15); p=0.002 <sup>#</sup>	1.04 (0.97-1.12); p=0.230	0.014

358

*Note*

359

<sup>#</sup> Statistically significant at Bonferroni corrected  $\alpha=0.007$ 

360

<sup>a</sup> On a scale from 0 (not stress at all) to 10 (extremely severe stress)

361

<sup>b</sup> Adjusted for all other predictor variables plus nationality, occupation, and number of pregnancies

362

363

Results of the main outcome measures “health influences on career choice”, “desired profession” and “professional experience” are highly significant; even if the proportion of variance explained by the last two factors was rather small. Excluding participants who are members of self-help groups did not alter the results.

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368

The intensity of reported health-related limitations in career choice was independent from rASRM-stage ( $\chi^2$ , 16.51, df=12, p=0.169), but associated with the occurrence of chronic pain ( $\chi^2$ , 34.39, df=4, p<0.001) as well as with the frequency of pain ( $\chi^2$ , 25.62, df=8, p=0.001).

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373

Chronic pain was also associated with higher levels of stress at work, even if the mean difference was small (6.61 vs 5.47, SD=2.39/2.49, p<0.001).

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3 375 Intraoperative findings of spread of endometriosis lesions showed varying  
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5 376 associations with health-related limitations in career choice: having endometriosis  
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7 377 lesions at the pelvic wall ( $\chi^2$ , 11.14,  $df=4$ ,  $p=0.025$ ) or in the sacrouterine ligaments  
8  
9 378 ( $\chi^2$ , 13.51,  $df=4$ ,  $p=0.009$ ) was significantly associated with greater limitations in  
10  
11 379 career choice, while such an outcome could not be found for localization in the  
12  
13 380 vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of stress  
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15 381 at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50,  
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17 382  $SD=2.46/2.48$ ,  $p=0.001$ ), but not with other intraoperative findings.  
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20 383

#### 21 22 384 **Work impairment and compensatory mechanisms**

23  
24 385 Asked about the amount of sick leave due to endometriosis during the last month,  
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26 386 78.1% of the women of the case group reported no sick leave, 8.5% reported one to  
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28 387 three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and  
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30 388 8.1% reported two to four weeks.

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32  
33 389 Altogether, 13.1% of endometriosis patients used one week or more of overtime or  
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35 390 vacation during the last year when they felt too sick to work due to symptoms of  
36  
37 391 endometriosis. Furthermore, 75.5% of women with endometriosis reported to have  
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39 392 gone to work during the previous month in spite of severe pain. Asked about the  
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41 393 previous year, 89.2% of women with endometriosis affirmed to have worked despite  
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43 394 pain. Out of the women diagnosed with endometriosis, 89.8% noted a loss of work  
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45 395 productivity due to endometriosis, with 65.1% reporting strong or very strong  
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47 396 limitations when symptoms were severe. On days with minimal endometriosis  
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49 397 symptoms, 75.3% still felt some degree of loss of productivity.

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51  
52 398 A minority of women with endometriosis reported working part time (10.3%) or giving  
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54 399 up work entirely (5.8%) due to their disease ( $n=445$ ).  
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3 401 **Association of endometriosis-related symptoms with sick leave and**  
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5 402 **productivity loss**

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7 403 We then examined whether different endometriosis symptoms were related to  
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9 404 absenteeism and impaired work productivity (Table IV).  
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11 405

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14 406 **Table IV: Association of endometriosis-related symptoms to sick leave and**  
15 407 **productivity loss in the last month**  
16 408

Predictor		Sick leave <sup>a</sup>		Productivity loss <sup>b</sup>	
		OR (95% CI)	R <sup>2</sup>	OR (95% CI)	R <sup>2</sup>
Chronic pain	Yes	3.52 (2.02; 6.13); p<0.001 <sup>#</sup>	0.072	3.08 (2.11; 4.50); p<0.001 <sup>#</sup>	0.087
	No	Ref.		Ref.	
Frequency of pain	Daily	2.82 (1.47; 5.39); p=0.002 <sup>#</sup>	0.053	1.81 (1.05; 3.12); p=0.032	0.040
	>1 per week	1.40 (0.66; 2.97); p=0.377		0.76 (0.42; 1.38); p=0.369	
	≤1 per week	Ref.		Ref.	
Frequency of fatigue	Frequently	3.50 (1.76; 6.94); p<0.001 <sup>#</sup>	0.073	3.99 (2.49; 6.39); p<0.001 <sup>#</sup>	0.107
	Sometimes	1.15 (0.50; 2.64); p=0.748		1.44 (0.86; 2.41); p=0.168	
	Rarely	Ref.		Ref.	
Psychological symptoms <sup>c</sup>	Yes	3.03 (1.77; 5.18); p<0.001 <sup>#</sup>	0.061	2.90 (1.98; 4.23); p<0.001 <sup>#</sup>	0.082
	No	Ref.		Ref.	

17 409 *Note*

18 410 <sup>#</sup> Statistically significant at Bonferroni corrected  $\alpha=0.01$

19 411 <sup>a</sup> Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days

20 412 <sup>b</sup> Refers to current maximal impairments; Scale: 1="not at all/little", 2="moderately/strong", 3="very strong"

21 413 <sup>c</sup> depressive mood/anxiety/reduced resilience of more than three months

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23 415 Corrected for multiple testing, all four predictor variables were significantly associated  
24 416 with sick leave during the previous four weeks. The occurrence of chronic pain as  
25 417 well as the frequency of fatigue and concomitant psychological symptoms were  
26 418 associated with significantly higher degrees of perceived productivity loss. Including  
27 419 age and time since diagnosis as potential confounders did not alter the results.  
28 420 Likewise, the factor of different localisations of endometriosis was not associated with  
29 421 sick leave or productivity loss (all p>0.05).  
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5 424 **Discussion**6  
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9 426 Endometriosis is associated with impairment of professional activity: women  
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11 427 diagnosed with endometriosis showed a lower likelihood of working in their desired  
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13 428 profession and stronger health-related limitations in their career decisions. In  
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15 429 contrast, they had professional experience of longer durations. All of these main  
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17 430 outcomes were not reported previously and open new insights into the professional  
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19 431 life of women with endometriosis. Endometriosis-associated symptoms and symptom  
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21 432 characteristics were moderately related to sick leave and loss of productivity, but in  
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23 433 contrast to our expectations, endometriosis was not associated with increased work-  
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25 434 related stress levels.

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31 436 In contrast to remarkable differences regarding parameters of working life, education  
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33 437 level did not differ significantly between case and control groups (Table I); this is a  
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35 438 result that has been described previously.<sup>17</sup> Other studies, however, reported serious  
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37 439 effects of endometriosis on education level, especially on tertiary formation.<sup>12 24</sup>  
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39 440 These contrasting findings might result from differences in study groups, e.g. with  
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41 441 regard to the onset of disease symptoms in relation to education, professional  
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43 442 training and professional activity. Many studies report an average age of first  
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45 443 symptoms between 20 and 29 years,<sup>10 38-40</sup>. In our study the average age of  
46  
47 444 diagnosis is 33.7 years. Even if many of these women report the onset of  
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49 445 endometriosis-related symptoms several years before diagnosis, it is still an age at  
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51 446 which most women have completed professional training. As a consequence, the  
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53 447 women investigated in such cohorts will not experience a negative impact of  
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55 448 endometriosis on their education, because they were still symptom-free at this age.

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3 449 Other authors reported an earlier onset of disease symptoms,<sup>41</sup> and emphasized that  
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5 450 endometriosis in adolescent girls was an underestimated problem.<sup>40 42 43</sup>

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7 451 Consequently, those women, which suffer from endometriosis symptoms already at a  
8  
9 452 young age, might feel limitations due to the disease also early in life, namely already  
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11 453 during education.

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13 454 On the other hand, there might be a higher tolerance for sick leave and impaired  
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15 455 energy levels in a school or university setting compared to in paid employment.

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19 457 Health issues are important criteria in career choice, and women diagnosed with  
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21 458 endometriosis do work less often in their desired profession. However, women with  
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23 459 endometriosis reported a greater length of experience in the current profession  
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25 460 (Table IIIb). Professional experience and the length of time a woman is working with  
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27 461 the current employer are highly correlated. These results can be interpreted  
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29 462 positively in the sense that women with endometriosis were successful in carefully  
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31 463 choosing a long-term profession. On the other hand, women might feel less able to  
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33 464 change the professional field and stuck in an undesired profession because of  
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35 465 endometriosis.

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39 467 Several authors reported elevated levels of general<sup>44 45</sup> as well as emotional<sup>21</sup>  
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41 468 distress in women diagnosed with endometriosis. This first study on work-specific  
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43 469 stress in endometriosis affected women produced results in contrast to our  
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45 470 expectations. Even though women reported that they sometimes went to work  
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47 471 despite endometriosis-associated pain, women with endometriosis did not  
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49 472 experience higher work-related stress levels than the control women; but within the  
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51 473 group of women with endometriosis, those with chronic pain reported significantly  
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53 474 higher work-related stress than those without pain. We investigated women whose

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3 475 initial diagnosis was up to 20 years ago; these women may have meanwhile found an  
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5 476 occupation meeting their needs, and superiors and colleagues may have adapted to  
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7 477 their sometimes reduced availability for work. Also, the fact that work can be a source  
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9 478 of distraction and of self-esteem for individuals suffering from a chronic disease<sup>46</sup>  
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11 479 may offset stressful situations.

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13 480 According to our results and those of others,<sup>41</sup> women affected by endometriosis  
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15 481 compensate for their health-related restrictions at work by using overtime or vacation  
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17 482 for absences as well as by saving energy for work through reduction of leisure time  
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19 483 activities.

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24 485 Despite these personal efforts to adapt to an adverse situation, productivity loss<sup>9 15</sup>  
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26 486 and sick leave<sup>9 10</sup> are relevant issues for many women diagnosed with endometriosis.

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28 487 Average loss of work time per week (absenteeism) due to endometriosis is reported  
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30 488 to be between 4.4 and 7.4 hours.<sup>13 14</sup> In our study, chronic pain, the frequency of

31  
32 489 pain, fatigue, and psychological symptoms, such as self-reported depression and  
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34 490 anxiety, were significantly - but with modest effect sizes - related to taking more sick

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36 491 leave (Table IV). Productivity loss at work due to endometriosis-related symptoms

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38 492 was described to be high or very high – depending on the current severity of

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40 493 symptoms – by up to 65% of women in the present study. Struggles to fulfil normal

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42 494 demands of work might be exacerbated by the side effects of treatment, for example

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44 495 by dizziness from strong pain killers.<sup>22 23</sup> Although, the majority of women affected

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46 496 with endometriosis seemed to be able to compensate for disease-related difficulties

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48 497 at work and to realize successful long-term professional activity, 16.2% of the women

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50 498 nevertheless reduced or even gave up work entirely due to endometriosis-related

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52 499 symptoms; this is a situation that has been observed also by others.<sup>17</sup> Furthermore, a

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54 500 very similar percentage of women with endometriosis and control women worked part

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3 501 time, even though women diagnosed with endometriosis remained childless more  
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5 502 often. Such decisions may result from feeling pressured to reduce or quit work when  
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7 503 employers know about a chronic disease such as endometriosis.<sup>12 24</sup> More flexible  
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9 504 work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted  
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11 505 physical demands, the possibility to lie down, and the existence of bathrooms nearby  
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13 506 are seen to be helpful resources for successful professional performance in women  
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15 507 with endometriosis.<sup>23 24</sup>

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20 509 As for the relationship between rASRM stage and endometriosis-associated  
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22 510 symptoms,<sup>1 3</sup> none of the parameters evaluating professional activity showed any  
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24 511 significant association with rARSM stage. Testing the association between different  
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26 512 intraoperative findings of endometriotic lesions and work outcomes showed  
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28 513 inconsistent results. In contrast, most outcome measures were related to the  
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30 514 occurrence and frequency of chronic pain; this result is supported by other studies on  
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32 515 endometriosis,<sup>14 19</sup> as well as on other chronic pain conditions such as migraine or  
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34 516 fibromyalgia.<sup>47 48</sup> Even if the effect size of pain on work in this study is limited,  
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36 517 findings support the relevance of pain management for satisfactory work  
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38 518 performance. Fatigue, either as a symptom of endometriosis or as a frequent  
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40 519 comorbidity,<sup>49</sup> interfered with professional activity in this as well as in other studies.<sup>1</sup>

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43 520 <sup>13</sup>

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46 521 In summary, it may be that women with endometriosis strive for normality at their  
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48 522 work place, even if it is associated with reduced professional flexibility or with giving  
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50 523 up the desire for another profession.

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55 525 This study presents one of the largest samples investigating the association between  
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57 526 endometriosis and professional life and it is one of the very few studies providing a

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3 527 control group. Study participants were recruited in university hospitals, in district  
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5 528 hospitals and in doctors' practices in order to collect a representative sample. The  
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7 529 pair matching with regard to age and ethnic background reduced the confounding  
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9 530 effect of these factors. A meticulous review of all surgical records by the same  
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11 531 investigator (AKS) ensured high data quality with regard to diagnosis and  
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13 532 classification of endometriosis. The response rate of 64.1% in the case group is in  
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15 533 the upper level of comparable studies,<sup>12 13</sup> whereas the response rate of 35.8% in the  
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17 534 control group is comparatively low. We cannot exclude that women with a particularly  
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19 535 high work load refrained from study participation; however, such an effect is equally  
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21 536 relevant in women diagnosed with endometriosis and in controls. The higher  
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23 537 response rate in women with endometriosis supports the fact that such an  
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25 538 association does not represent a particular problem for members in this group.

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28 539 Given the methodology of a self-reported questionnaire answered retrospectively,  
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30 540 distortions in the sense of falsely or overly attributing dissatisfaction on the job to  
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32 541 endometriosis cannot be excluded. By addressing questions on professional activity  
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34 542 either current or in the period just prior to study participation, we tried to reduce recall  
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36 543 bias. As we included only patients with a confirmed diagnosis of endometriosis, and  
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38 544 as such a confirmation can be provided only by surgery, there may be referral bias.  
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40 545 For example, affected but asymptomatic women and symptomatic women who do  
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42 546 not have access to or refused surgery might have been excluded, with the first false  
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44 547 categorization might result in over- and the second in underestimation of the results.  
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46 548 In contrast, asymptomatic women with endometriosis might have been included in  
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48 549 the control group which would result in underestimation of results. As we have no  
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50 550 differentiated information on symptoms resulting from diseases other than  
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52 551 endometriosis, in both groups further confounders might be present; this would also  
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54 552 result in underestimation of our findings. Although we recruited women diagnosed  
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3 553 with endometriosis independent from their acute symptomatology e.g. also those  
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5 554 presenting for regular controls, recruitment through hospitals might have resulted in  
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7 555 selection of women with more severe disease symptoms. A comparison group for the  
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9 556 questions of sick leave and productivity loss at work would have been beneficial.  
10  
11 557 However, analysis of impact of different endometriosis-related symptoms on these  
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13 558 two outcomes allowed for indirect conclusions on the association between  
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15 559 endometriosis and reduced working ability, as well as basic data to design future  
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17 560 studies.  
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### 563 **Conclusion**

564 Even if most measured effect sizes of associations between endometriosis and  
565 individual parameters of working life were small, the study indicates a burdensome  
566 influence of the disease on the working life of women affected by endometriosis.  
567 Therefore, medical and psychological support should be sensitised towards such  
568 issues in order to support women in managing their working life and adjusting their  
569 professional choices and professional development to individual endometriosis-  
570 related conditions if needed. Furthermore, for professionals in occupational medicine,  
571 insurances, politics etc. it might be useful to know about endometriosis-related  
572 challenges and possible limitations in professional activity.  
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8  
9 582 manuscript.

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18 586 **Authors roles**

19  
20 587 MLS: collection of data on site in Solothurn and Schaffhausen, interpretation of data,  
21  
22 588 drafting and finalization of the manuscript

23  
24 589 MPH: statistical analysis, interpretation of data, finalization of manuscript

25  
26 590 AKS: investigator, collection of data on site in Winterthur, Switzerland, verification of  
27  
28 591 surgical reports, finalization of the manuscript

29  
30 592 KG: concept of study, collection of data on site in Zurich, management databank,  
31  
32 593 finalization of the manuscript

33  
34 594 MR: investigator, collection of data on site in Berlin, Germany, finalization of the  
35  
36 595 manuscript

37  
38 596 MW: investigator, collection of data on site in Aachen, Germany, and in Graz,  
39  
40 597 Austria, finalization of the manuscript

41  
42 598 FH: investigator, collection of data on site in St. Gallen, Switzerland, finalization of  
43  
44 599 the manuscript

45  
46 600 SvO: investigator, collection of data on site in Zurich, Switzerland, finalization of the  
47  
48 601 manuscript

49  
50 602 ME: investigator, collection of data on site in Schaffhausen, Switzerland, finalization  
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52 603 of the manuscript

1  
2  
3 604 FM: concept of study, investigator on site in Solothurn, Switzerland, finalization of  
4  
5 605 manuscript  
6  
7 606 BI: concept of study, investigator on site in Zurich, Switzerland, interpretation of data,  
8  
9 607 finalization of manuscript  
10  
11 608 PI: concept of study, investigator and data collection in Zurich, Switzerland,  
12  
13 609 finalization of the manuscript  
14  
15 610 BL: principal investigator, concept and conduct of study, investigator on site in Zurich,  
16  
17 611 Switzerland, collection and analysis of data, preparation and finalization of  
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19 612 manuscript  
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13 738 work productivity. *J Occup Environ Med* 2011;53:765-770.

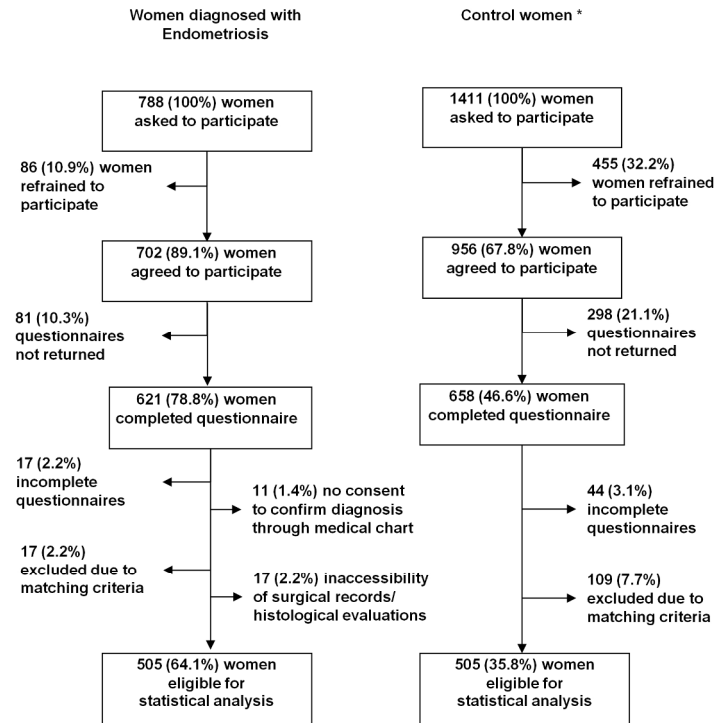
14  
15 739 49 Sinaii N, Cleary SD, Ballweg ML, et al. High Rates of Autoimmune and Endocrine  
16  
17 740 Disorders, Fibromyalgia, Chronic Fatigue Syndrome and Atopic Diseases among  
18  
19 741 Women with Endometriosis: A Survey Analysis. *Hum Reprod* 2002;17:2715-2724.

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23  
24 743 **Figure Legend**

25  
26 744 Fig 1.: Recruitment of study participants  
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Flow chart I. Recruitment of study participants



\* women presenting for routine gynaecological care or benign gynaecological surgery

190x274mm (284 x 284 DPI)

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8/9
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	7

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.  
**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).



# BMJ Open

## Does endometriosis affect professional life? – a matched case-control study in Switzerland, Germany and Austria

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<b>Primary Subject Heading</b>:	Obstetrics and gynaecology
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Keywords:	Endometriosis, work, professional life, pain, stress, career choice

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Manuscripts

# 1 Does endometriosis affect professional life? – 2 a matched case-control study in Switzerland, 3 Germany and Austria

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24  
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1  
2  
3 35 **Abstract**  
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5 36 **Objectives:** Endometriosis is a gynaecological disease most commonly causing  
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8 37 severe and chronic pelvic pain as well as an impaired quality of life. The aim of this  
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11 38 study was to investigate if and how endometriosis affects choices regarding  
12  
13 39 professional life as well as the quality of daily working life.  
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16 40 **Design, setting, and participants:** In the context of a multicentre case-control  
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18  
19 41 study, we collected data from 505 women with surgically/histologically confirmed  
20  
21 42 diagnosis of endometriosis and 505 matched controls. Study participants were  
22  
23 43 recruited prospectively in hospitals and doctors' practices in Switzerland, Germany,  
24  
25 44 and Austria. Using a detailed questionnaire, the study investigated work-life and  
26  
27 45 career choices of study participants.  
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29

30 46 **Main outcome measures:** Associations between endometriosis/ disease symptoms  
31  
32 47 and limitations in career development as well as ability to work.  
33

34 48 **Results:** Women with endometriosis were less often able to work in their desired  
35  
36  
37 49 profession than women from the control group (adjusted OR=1.84, 95%-CI: 1.15-  
38  
39 50 2.94,  $R^2=0.029$ ,  $p=0.001$  and they had to take health-related limitations into  
40  
41 51 consideration in their career decisions to a significantly higher degree than women in  
42  
43 52 the control group (aOR=4.79, 95%-CI: 2.30-9.96,  $R^2=0.063$ ,  $p<0.001$ ). Among  
44  
45 53 women with endometriosis, chronic pain was significantly associated with increased  
46  
47 54 sick leave (OR=3.52, 95%-CI: 2.02-6.13,  $R^2=0.072$ ,  $p<0.001$ ) as well as with loss of  
48  
49 55 productivity at work (OR=3.08, 95%-CI: 2.11-4.50,  $R^2=0.087$ ,  $p<0.001$ ).  
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53 56 **Conclusions:** Endometriosis is associated with impairment of professional life, in  
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56 57 particular with regard to career choices. Further research to develop strategies to  
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3 58 support endometriosis-affected women in realizing professional opportunities is  
4  
5 59 recommended.

### 60 **Strengths and limitations of this study**

61 The study presents one of the largest samples and is one of the first studies  
62 providing a matched control group to investigate the association between  
63 endometriosis and professional activity.

64 Recruitment of study participants in university hospitals, in district hospitals and in  
65 private doctors' practices ensures a representative sample.

66 Validation of diagnosis and stage of endometriosis provides high data quality.

67 The use of a self-reported questionnaire may have caused recall bias.

68 Due to lack of investigation of diseases or symptoms that may also have influenced  
69 professional life in the control group, results may be underestimated.

70

### 71 **Trial registration number**

72 Clin.trial.gov: Endo\_QOL NCT02511626

73

### 74 **Funding**

75 This research received no specific grant from any funding agency in the public,  
76 commercial, or not-for-profit sectors.

77

### 78 **Conflict of interest**

79 The authors do not have any competing interests.

80

### 81 **Data sharing statement**

82 The data set is available on request from the corresponding author.

83

84 **Key words:** Endometriosis, work, professional life, stress, career choice

85

86

## 87 **Introduction**

88

89 Endometriosis is a gynaecological disease defined by the presence of endometrium-  
90 like tissue outside the uterine cavity.<sup>1</sup> The prevalence of the disease among women  
91 of reproductive age is estimated to be between 8 and 10%.<sup>2 3</sup> However, as reliable  
92 diagnosis of endometriosis can only be made by surgery and endometriosis can be  
93 asymptomatic, an unknown number of affected women might remain undiagnosed  
94 e.g. prevalence might be far higher.<sup>4</sup>

95

96 Women suffering from endometriosis experience most commonly one or more of the  
97 following symptoms: chronic pelvic pain, severe dysmenorrhea, deep dyspareunia,  
98 pain during defecation/urination, loin pain, irregular bleeding, constipation/diarrhoea,  
99 as well as reduced fertility and chronic fatigue.<sup>5 6 7</sup> Numerous and severe symptoms,  
100 the chronicity of the disease<sup>8</sup>, side effects of therapies<sup>9</sup> as well as diagnostic delays<sup>10</sup>  
101 <sup>11</sup> significantly affect women's overall quality of life, including professional  
102 performance, and place high demands on the treating physicians.<sup>12 13 14</sup> For most  
103 patients, available treatment options, such as analgesics, various hormonal  
104 therapies, and radical laparoscopy<sup>1</sup> are often not curative and are associated with  
105 significant side effects.<sup>12 15</sup>

106 Consequently, disease symptoms, especially endometriosis-related pain and fatigue,  
107 may disturb the development and realization of long-term goals such as a  
108 professional career<sup>16</sup> and may make it difficult to meet the demands of a job. About  
109 40% of women with endometriosis report impaired career growth due to

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2  
3 110 endometriosis,<sup>13</sup> and about 50% experience a decreased ability to work due to their  
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5 111 chronic disease.<sup>12 17</sup> Differentiated knowledge on the nature of such limitations and in  
6  
7 112 particular on how adjustments to professional life can be made to improve  
8  
9 113 professional performance is currently lacking.

10  
11 114 The quality of working life is a major aspect in quality of life overall,<sup>18</sup> which in turn is  
12  
13 115 the most important predictor of total cost of disease.<sup>19</sup> About 66% to 75% of the total  
14  
15 116 costs of endometriosis arise from reduced ability to work and not from direct costs of  
16  
17 117 treatment.<sup>19 20</sup> Being able to work in a desired occupation may not only have a strong  
18  
19 118 impact on a woman's financial situation and on the perception of and attitude toward  
20  
21 119 daily work, but can also be an important health factor. For example, unsatisfactory  
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23 120 work and limited possibilities for change are associated with increased levels of  
24  
25 121 headache, fatigue and depressed mood.<sup>21</sup>

26  
27  
28  
29 122 Frequent sick leave and reduced work productivity can put affected women under  
30  
31 123 observation by superiors and under greater pressure to deliver full performance.<sup>22 23</sup>

32  
33 124 The rather intimate and gender-specific nature of the most common endometriosis  
34  
35 125 symptoms tends to make affected women feel embarrassed.<sup>24</sup> Consequently, some  
36  
37 126 women may avoid discussing endometriosis-related problems with superiors and  
38  
39 127 colleagues, particularly if the superiors and colleagues are male.<sup>24 25</sup> Due to the  
40  
41 128 invisibility of their disease, women can be easily perceived as malingerers.<sup>24</sup>

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43  
44 129 Therefore, medical professionals need to know how the symptoms of endometriosis  
45  
46 130 can affect daily working life and professional development, notably because  
47  
48 131 endometriosis-affected women repeatedly underline their wish for comprehensive  
49  
50 132 information<sup>24 26 27</sup> and advice in managing their disease in daily life,<sup>26 27</sup> instead of  
51  
52 133 isolated treatment of endometriosis symptoms.<sup>24 26 27</sup> A better understanding of  
53  
54 134 endometriosis and its impacts on any aspect of life - including professional activity -  
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56  
57 135 not only by medical professionals but also in society and politics would help affected

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3 136 women and their families to reduce negative consequences of the disease. However,  
4  
5 137 research on quantitative and qualitative impairment of working life as the necessary  
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7 138 background for offering adequate support and interventions is scarce and relies  
8  
9 139 mainly on interview-based studies with small samples of affected women<sup>23 24</sup>; there is  
10  
11 140 only one other study that uses a control group.<sup>14</sup> In addition, work-related stress in  
12  
13 141 women diagnosed with endometriosis has not been investigated yet.

14 142 Therefore, it was the aim of the present study to investigate parameters of working  
15  
16 143 life of a larger number of endometriosis-affected women, and compare findings with  
17  
18 144 those of a matched control group. We investigated (i) perceived health-related  
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20 145 limitations in career decisions; (ii) quality of the current work situation; and (iii) the  
21  
22 146 association between endometriosis-related disease symptoms and work  
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24 147 performance.  
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## 30 31 149 **Material and Methods**

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### 35 36 151 **Study design**

37  
38 152 The study is designed as a multicentre case-control study. Main outcome measures  
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40 153 are health limitations in career choice as well as quality and stability of the current  
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42 154 work situation. Secondary outcome measures investigate the impact of different  
43  
44 155 symptoms as well as localisation of endometriosis on sick leave and loss of  
45  
46 156 productivity. The study has been conducted and reported applying the criteria of the  
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48 157 STROBE Statement.<sup>28</sup>  
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### 52 53 159 **Recruitment**

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3 160 Recruitment of study participants is shown in Figure I. To detect a 10% difference  
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5 161 between cases and controls with an alpha of 0.05, and a power of 0.8 a sample size  
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7 162 of 387 participants in each group is needed. With the inclusion of 505 participants in  
8  
9 163 both groups we consequently reached very high power, for example 99.1 for the  
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11 164 detection of differences in desired profession or 99.7 for health-related limitations in  
12  
13 165 career choice. Study participants were recruited prospectively for a research project  
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15 166 on quality of life including professional activity in endometriosis-affected women  
16  
17 167 compared to control women.<sup>7 9 29 30 31</sup> Recruitment took place between January 2010  
18  
19 168 and December 2015 at the following hospitals and associated doctors' offices in  
20  
21 169 Switzerland, Germany and Austria: the University Hospital Zurich, the Triemli  
22  
23 170 Hospital Zurich, the district hospitals in Schaffhausen, Solothurn, St. Gallen,  
24  
25 171 Winterthur, Baden, and Walenstadt, the Charité Berlin, the Vivantes Humboldt  
26  
27 172 Hospital Berlin, the Albertinen Hospital Hamburg, the University Hospital Aachen,  
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29 173 and the University Hospital Graz. In doctors' offices one or several gynecologists  
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31 174 work together in a medical unit; district hospitals offer tertiary care associated with a  
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33 175 university.  
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37 176 Healthcare professionals carried out the recruitment of all study participants via direct  
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39 177 approach. The study was explained to the respondents and information about the  
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41 178 voluntary nature of participation as well as anonymity of data in reports and  
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43 179 publications was provided. Each participant received a detailed written description of  
44  
45 180 the study and signed informed consent. Participants were given all documents and a  
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47 181 return envelope.  
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50 182 Inclusion criteria: All study participants had to be between 18 and 50 years old. For  
51  
52 183 the case group, women with surgically and histologically diagnosed endometriosis  
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54 184 were included irrespective of stage, location of lesions, and severity and profile of  
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56 185 symptoms. Only data sets with at least 80% of answers for main and secondary



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3 186 outcome measures were included.

4  
5 187 Exclusion criteria: Women were excluded in cases of current pregnancy or linguistic,  
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7 188 mental or psychological impairments that might affect their ability to understand and  
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9 189 to complete the questionnaire.

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11 190 The most frequent reasons reported for not participating were lack of time and the  
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13 191 intimate nature of some of the questions. To maximize the return rate, women were  
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15 192 reminded to complete and return the questionnaire after one month and after three  
16  
17 193 months.

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20 194 A smaller segment of the case group (N=74, 66 of which could be included in the  
21  
22 195 final analysis (13.1% of total case group)) was recruited through different self-help  
23  
24 196 groups for endometriosis patients (in Germany only). Education levels and family  
25  
26 197 incomes in this cohort are similar to those in the main group. However, the women in  
27  
28 198 this cohort were significantly older than those in the hospital group ( $42.45 \pm 6.03$   
29  
30 199 versus  $37.02 \pm 7.21$  years,  $p < 0.001$ ), showed a longer time since primary diagnosis  
31  
32 200 ( $82.11 \pm 8.36$  versus  $37.20 \pm 44.00$  months,  $p < 0.001$ ), and presented at the time of the  
33  
34 201 study a significantly higher stage of disease ( $p = 0.013$ ).

35  
36  
37 202 Control women were recruited during regular annual or biennial gynaecological  
38  
39 203 consultations at hospitals' out-patient clinics or in private offices, as part of standard  
40  
41 204 healthcare in the three countries where recruitment took place. In addition, women  
42  
43 205 during hospital stays because of temporary mild benign gynaecological problems  
44  
45 206 other than endometriosis were invited to participate in the study. Each control woman  
46  
47 207 was matched to a woman diagnosed with endometriosis for age ( $\pm 3$  years) and  
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49 208 ethnic background, i.e. Caucasian or not (pair matching).

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55 210 **Questionnaire**

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3 211 The structured self-administered questionnaire for the total study on quality of life  
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5 212 contained 390 questions for all participants and 90 additional specific questions for  
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7 213 women diagnosed with endometriosis. It is structured in different chapters, one of  
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9 214 which is professional life. Further chapters covered questions regarding life style;  
10  
11 215 general wellbeing; general, gynaecological, and medical history; childhood  
12  
13 216 experiences; sexuality and partnership. Women diagnosed with endometriosis were  
14  
15 217 additionally asked to provide detailed information on the diagnosis and treatment of  
16  
17 218 endometriosis, symptoms of endometriosis, sick leave, and productivity loss due  
18  
19 219 specifically to endometriosis. Wherever possible we used internationally validated  
20  
21 220 questionnaires. Modified versions of the Brief Pain Inventory<sup>32</sup> and the Pain Disability  
22  
23 221 Index<sup>33 34</sup> served to evaluate pain. For several questions about professional life as for  
24  
25 222 occupation, sick leave and productivity loss, we used similar reporting methods the  
26  
27 223 WPAI<sup>35</sup> suggests, but extended the time period of reporting from only seven days in  
28  
29 224 the WPAI to four weeks and one year. Level of education was measured with defined  
30  
31 225 categories following the recommendation to use meaningful benchmarks of  
32  
33 226 educational attainment rather than a continuous scale in years.<sup>36</sup> In order to capture  
34  
35 227 the professional situation of women diagnosed with endometriosis as close to reality  
36  
37 228 as possible a interdisciplinary research team including specialists for minimally  
38  
39 229 invasive endometriosis-surgery, for gynaecological endocrinology and for gynaeco-  
40  
41 230 psychosomatic medicine added their clinical experience and evaluated systematically  
42  
43 231 what they had learned from individual patients. On this background specific questions  
44  
45 232 like on working despite pain or on using overtime or holidays to compensate for sick  
46  
47 233 leave were added. The first version of our questions on professional activity was than  
48  
49 234 revised by the governing body of the German self-help groups in order to map the  
50  
51 235 questions to the situations reported by women with endometriosis and to avoid using  
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3 236 questions, which do not correctly depict the specific situation in the context of  
4  
5 237 endometriosis.

6  
7 238 The analysis presented in this paper was based on answers to the following  
8  
9 239 questions asked to the case as well as to the control group: nationality (German,  
10  
11 240 Swiss, Austrian, other [with the possibility of entering nationality]), age (years),  
12  
13 241 marital status (married/cohabiting/single), highest achieved education level (lower  
14  
15 242 school education, high school education, apprenticeship, university degree, no formal  
16  
17 243 education, other), current own monthly net income (six choices for responses ranging  
18  
19 244 from none to >2500 Euros for participants in Germany and Austria and from none to  
20  
21 245 >6000 Swiss francs for participants in Switzerland), numbers of pregnancies of more  
22  
23 246 than 24 weeks of gestation. Women were asked to report their levels of current  
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25 247 employment (full-time/part-time/full-time housekeeping/student/registered as  
26  
27 248 unemployed) and whether they currently worked in their desired profession (yes/no).  
28  
29 249 This question does not ask about the current place of employment but on the  
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31 250 profession itself, e.g. for a woman who always wanted to be a teacher, is she now  
32  
33 251 able to work as a teacher? They were asked how they perceived their level of  
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35 252 qualification for the currently held job (overqualified, about right, under-qualified),  
36  
37 253 length of professional experience (<5 years, 6-10 years, and >10 years), years  
38  
39 254 working with the current employer (<1 year, 1-5 years, 6-10 years, >10 years), the  
40  
41 255 subjectively perceived influence of health-related limitations on career choice (not at  
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43 256 all, little, medium, strongly, exclusively) and perceived current level of stress on the  
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45 257 job (scale from 0=none to 10=very strong).

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49  
50 258 The analysis presented in this paper further used the following questions asked only  
51  
52 259 to women diagnosed with endometriosis: Amount of time since first symptoms of  
53  
54 260 endometriosis were noticed (<1 year ago/1 year ago/2-5 years ago/6-10 years  
55  
56 261 ago/>10 years ago), date of initial diagnosis of endometriosis (month and year),  
57  
58  
59  
60

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2  
3 262 number of surgeries related to endometriosis (1/2/3/4/5/6 or more), chronic pain  
4  
5 263 (yes/no), duration of pain (<1 year/1-3 years/4-5 years/6-10 years/11-20 years/>20  
6  
7 264 years), frequency of pain (a few times per year/a few times per month/several times  
8  
9 265 per week/once a day/several times a day/permanently), cyclic pain (yes/no),  
10  
11 266 psychological symptoms lasting more than three months estimated by the study  
12  
13 267 participant to be related to endometriosis, such as depressive mood/anxiety/reduced  
14  
15 268 resilience (yes/no), days worked despite pain during the last month (never/1-3  
16  
17 269 days/4-7 days/1-2 weeks/2-4 weeks), frequency of fatigue or exhaustion due to  
18  
19 270 endometriosis (never/rarely/sometimes/often/very often), sick leave due to symptoms  
20  
21 271 of endometriosis (not specified) during the last month (never/1-3 days/4-7 days/1-2  
22  
23 272 weeks/2-4 weeks), sick leave due to symptoms of endometriosis in the last year  
24  
25 273 (never/1-7 days/1-2 weeks/2-4 weeks/4-8 weeks/8-12 weeks/>12 weeks), estimated  
26  
27 274 loss of productivity due to endometriosis when symptoms are at their maximum or at  
28  
29 275 their minimum respectively (no loss/a little/somewhat/high), reduction of work time  
30  
31 276 due to endometriosis (no reduction/reduction of 25%/50%/75%), and giving up  
32  
33 277 employment entirely due to endometriosis (yes/no). (Chronic pelvic pain included  
34  
35 278 cyclic as well as non-cyclic pelvic pain.)  
36  
37  
38  
39 279 The study was registered at clinicaltrials.gov (NCT 02511626), where further details  
40  
41 280 on the complete questionnaire are available.  
42  
43  
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45

281

## 282 **Verification of diagnosis and stage of endometriosis**

283 To verify diagnosis and obtain information about localization of endometriosis  
284 lesions, surgical records as well as the histological diagnosis of each patient and  
285 each intervention were collected from medical charts. Stage was classified according  
286 to the revised Classification of the American Society for Reproductive Medicine  
287 (rASRM).<sup>37</sup>

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4  
5 289 **Ethical approval**

6  
7 290 The study was approved by the Swiss ethics commission as well as by the ethics  
8  
9 291 boards of participating hospitals. This study followed the guidelines of the World  
10  
11 292 Medical Association Declaration of Helsinki 1964, updated in October 2013.

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13  
14 293

15  
16 294 **Patient and Public Involvement statement**

17  
18 295 Questions for this study were selected in cooperation with endometriosis self-help  
19  
20 296 groups. Other than in the self-help groups patients were not involved in the  
21  
22 297 recruitment and conduct of the study. All interested study participants receive the  
23  
24 298 publications resulting from the study. Publications are also sent to the governing  
25  
26 299 body of the self-help groups.

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30  
31 301 **Statistical analysis**

32  
33 302 Differences in sample characteristics between study groups were computed with  
34  
35 303 either independent sample t-tests for continuous variables or Pearson  $\chi^2$ -tests for  
36  
37 304 categorical variables. To test associations between study groups and characteristics  
38  
39 305 of professional life, we conducted a series of binomial logistic regression. The study  
40  
41 306 group, i.e. women with endometriosis as opposed to controls without endometriosis,  
42  
43 307 was included as the dependent variable. To test association between symptoms of  
44  
45 308 endometriosis and work outcomes in women with endometriosis, we conducted a  
46  
47 309 series of ordinal logistic regression, entering work outcomes as the dependent  
48  
49 310 variable. The proportion of variance explained based on the study group was  
50  
51 311 indicated by Nagelkerke's pseudo  $R^2$ . Sample characteristics that differed  
52  
53 312 significantly between study groups were statistically adjusted for by including them  
54  
55 313 simultaneously as covariates. Initially,  $\alpha$  was set at 5%, but we applied Bonferroni

314 correction to adjust the significance level  $\alpha$  for multiple testing. All analyses were  
 315 conducted with SPSS version 24 for Windows.

316

## 317 Results

318

### 319 Characteristics of study groups and possible confounders

320 A comparison of socio-epidemiological parameters between women with  
 321 endometriosis and control women is presented in Table I. Significant variables, eg  
 322 nationality, pregnancies, and paid employment, were included as covariates in  
 323 subsequent analyses on case-control effects.

324

325 **Table I: Descriptive statistics and group comparisons**

		Endometriosis (N=505)	Controls (N=505)	Group differences
Age	Mean years (SD)	37.7 (7.3)	37.2 (9.1)	p=0.344 <sup>a</sup>
Nationality	Swiss German Others	N=211 (42.2%) N=244 (48.8%) N=45 (9.0%)	N=285 (57.3%) N=161 (32.4%) N=51 (10.3%)	p<0.001 <sup>b</sup>
Marital status	Married/ Cohabiting Single	N=420 (83.3%) N=84 (16.7%)	N=397 (79.4%) N=103 (20.6%)	p=0.109 <sup>b</sup>
Pregnancies >24 weeks	0 1 ≥2	N=331 (70.6%) N=83 (17.7%) N=55 (11.7%)	N=245 (50.9%) N=80 (16.6%) N=156 (32.4%)	p<0.001 <sup>b</sup>
Education level <sup>c</sup>	Low Medium High	N=71 (14.4%) N=245 (49.6%) N=178 (36.0%)	N=74 (14.7%) N=249 (49.4%) N=181 (35.9%)	p=0.990 <sup>b</sup>
Paid occupation	Full-time Part-time None	N=248 (49.8%) N=176 (35.3%) N=74 (14.9%)	N=206 (41.8%) N=186 (37.7%) N=101 (20.5%)	p=0.016 <sup>b</sup>
Occupation among mothers <sup>d</sup> only	Full-time Part-time None	N=30 (22.1%) N=68 (50.0%) N=38 (27.9%)	N=57 (23.9%) N=136 (57.1%) N=45 (18.9%)	p=0.120 <sup>b</sup>

326 Note

327 <sup>a</sup> Independent samples t-test

328 <sup>b</sup> Pearson  $\chi^2$ -test

329 <sup>c</sup> Scale: Low="no formal education/lower school education", Medium="higher school education/apprenticeship",

330 High="university degree"

331 <sup>d</sup> women with at least one pregnancy >24 weeks

332

333 Disease characteristics of the endometriosis group are shown in Table II.

334 **Table II: Disease characteristics in women diagnosed with endometriosis**

Criteria		Endometriosis Group %	N
Time since occurrence of first symptoms (N=474)	<1 year	5.49%	26
	1 year	5.27%	25
	2-5 years	28.06%	133
	6-10 years	18.99%	90
	>10 years	42.19%	200
rASRM-stage of endometriosis (N=502)	I	17.93%	90
	II	21.12%	106
	III	28.09%	141
	IV	32.87%	165
Number of endometriosis-related surgical interventions (N=505)	1	49.31%	249
	2	29.11%	147
	3	7.13%	36
	4	2.77%	14
	5	2.18%	11
	6 and more	2.18%	11
	No information <sup>a</sup>	7.33%	37
	Mean±SD	1.79±1.27	
Douglas obliteration (N=503)	Yes	26.6%	134
	No	73.4%	369
Involvement of sacrouterine ligaments (N=503)	Yes	61.4%	309
	No	38.6%	194
Involvement of Douglas (N=503)	Yes	72.0%	362
	No	28.0%	141
Intra-abdominal adhesions (N=504)	Yes	74.8%	377
	No	25.2%	127
Involvement of pelvic wall (N=503)	Yes	74.8%	377
	No	25.2%	127
Involvement of vaginal fornix or septum rectovaginal (N=503)	Yes	12.7%	64
	No	87.3%	439
Endometrioma (N=502)	Yes	49.0%	246
	No	51.0%	256
Chronic pain (N=500)	Yes	58.40%	292
	No	41.60%	208
Duration of chronic pain	<1 year	3.48%	10
	1-3 years	13.59%	39
	4-5 years	17.07%	49
	6-10 years	23.34%	67
	11-20 years	29.27%	84
	>20 years	13.24%	38

<b>Frequency of pain</b>	Permanent	17.06%	51
	Several times per day	20.40%	61
	Once a day	1.34%	4
	Several times per week	26.76%	80
	Few times per month	31.77%	95
	Few times per year	2.68%	8
<b>Frequency of endometriosis-related fatigue/ exhaustion</b>	Never	7.39%	37
	Rarely	15.57%	78
	Sometimes	26.35%	132
	Often	28.14%	141
	Very often	22.55%	113
<b>Psychological Symptoms due to endometriosis<sup>b</sup></b>	Yes	57.24%	261
	No	42.76%	195

335 *Note*

336 <sup>a</sup> question not answered but diagnosis of endometriosis confirmed with at least one surgical record

337 <sup>b</sup> depressive mood/anxiety/reduced resilience of more than three months

338

### 339 **Parameters of working life**

340 Parameters of professional activity in women diagnosed with endometriosis and  
341 control women are presented in Table IIIa.

342

### 343 **Table IIIa: Parameters of professional activity in the case and the control group**

Criteria	Endometriosis group	N	Control group	N
<b>Own net income per month</b>		<b>480</b>		<b>483</b>
No income	11.25%	54	15.76%	76
<3000 CHF (1000 EUR) <sup>a</sup>	24.79%	119	28.57%	138
3001-6000 CHF (1001-2500 EUR) <sup>a</sup>	49.17%	236	40.37%	195
>6000 CHF (>2500 EUR) <sup>a</sup>	14.79%	71	15.32%	74
<b>Desired profession</b>		<b>488</b>		<b>482</b>
Yes	51.64%	252	64.94%	313
No	25.41%	124	14.94%	72
Partially	22.95%	112	20.12%	97
<b>Degree of health-related limitations in career choice</b>		<b>486</b>		<b>466</b>
Exclusively	4.12%	20	0.43%	2
Strongly	8.02%	39	3.00%	14
Somewhat	10.49%	51	4.94%	23
Little	8.23%	40	5.15%	24
Not at all	69.14%	336	86.48%	403
<b>Estimation of adequacy of job qualification</b>		<b>459</b>		<b>453</b>
Lower than required	19.17%	88	17.00%	77
Same as required	67.10%	308	74.61%	338
Higher than required	13.73%	63	8.39%	38
<b>Professional experience</b>		<b>487</b>		<b>474</b>



<5 years	18.89%	92	32.70%	155
5-10 years	25.87%	126	21.10%	100
>10 years	55.24%	269	46.20%	219
<b>Duration of current employment</b>		<b>442</b>		<b>439</b>
<1 year	14.25%	63	20.27%	89
1-5 years	40.72%	180	41.69%	183
6-10 years	22.17%	98	18.91%	83
>10 years	22.85%	101	19.13%	84
<b>Work-related stress level</b>		<b>460</b>		<b>465</b>
No stress	2.83%	13	1.51%	7
1	3.26%	15	2.80%	13
2	4.13%	19	5.16%	24
3	5.00%	23	10.54%	49
4	7.39%	34	9.46%	44
5	13.70%	63	14.624%	68
6	12.83%	59	14.194%	66
7	18.70%	86	20.430%	95
8	16.96%	78	14.624%	68
9	6.96%	32	2.796%	13
Very high stress	8.26%	38	3.871%	18

344 Note

345 <sup>a</sup> different income classes in Switzerland and Germany/ Austria

346 Spearman correlation between professional experience and length of time in the  
 347 current employment was  $r=0.490$  ( $p<0.001$ ).

348

349 Associations between endometriosis and work outcomes are presented in Table IIIb.

350 In the adjusted analysis, all predictor variables plus nationality, occupation and  
 351 number of pregnancies were included simultaneously as covariates.

352

353 **Table IIIb: Associations between endometriosis and parameters of pro-**  
 354 **fessional life including the proportion of variance explained by the disease**

Predictor	Reference category	Unadjusted OR (95% CI)	Adjusted OR (95% CI) <sup>b</sup>	Pseudo R <sup>2</sup>
Own income	0-3000 CHF	0.85 (0.58-1.24); $p=0.396$	1.01 (0.56-1.83); $p=0.975$	0.011
	3001-6000 CHF	1.26 (0.87-1.84); $p=0.227$	1.23 (0.78-1.96); $p=0.376$	
	>6000 CHF	Ref.	Ref.	
Desired profession	No	2.14 (1.53-2.99); $p<0.001^{\#}$	1.84 (1.15-2.94); $p=0.011$	0.029
	Partially	1.43 (1.04-1.97); $p=0.026$	1.51 (1.02-2.23); $p=0.038$	
	Yes	Ref.	Ref.	
Degree of health-related limitations in career choice	Strongly	4.42 (2.50-7.83); $p<0.001^{\#}$	4.79 (2.30-9.96); $p<0.001$	0.063
	Moderately	2.32 (1.59-3.40); $p<0.001^{\#}$	2.61 (1.64-4.15); $p<0.001$	
	Not at all	Ref.	Ref.	
Estimation of adequacy of job qualification	Lower	1.25 (0.89-1.77); $p=0.195$	0.86 (0.55-1.35); $p=0.515$	0.012
	Higher	1.82 (1.18-2.80); $p=0.007^{\#}$	1.44 (0.87-2.41); $p=0.160$	
	Adequate	Ref.	Ref.	
Professional	<5 years	0.48 (0.35-0.66); $p<0.001^{\#}$	0.44 (0.28-0.71); $p=0.001$	0.033

experience	5-10 years >10 years	1.03 (0.75-1.41); p=0.875 Ref.	1.02 (0.67-1.57); p=0.916 Ref.	
Duration of current employment	<1 year	0.59 (0.38-0.91); p=0.017	0.84 (0.47-1.50); p=0.552	0.011
	1-5 years	0.82 (0.57-1.17); p=0.268	1.14 (0.71-1.84); p=0.584	
	6-10 years	0.98 (0.65-1.48); p=0.931	0.99 (0.60-1.65); p=0.975	
	>10 years	Ref.	Ref.	
Work-related stress level	1 point increase <sup>a</sup>	1.09 (1.03-1.15); p=0.002 <sup>#</sup>	1.04 (0.97-1.12); p=0.230	0.014

Note

<sup>#</sup> Statistically significant at Bonferroni corrected  $\alpha=0.007$

<sup>a</sup> On a scale from 0 (not stress at all) to 10 (extremely severe stress)

<sup>b</sup> Adjusted for all other predictor variables plus nationality, occupation, and number of pregnancies

Results of the main outcome measures “health influences on career choice”, “desired profession” and “professional experience” are highly significant; even if the proportion of variance explained by the last two factors was rather small. Excluding participants who are members of self-help groups did not alter the results.

The intensity of reported health-related limitations in career choice was independent from rASRM-stage ( $\chi^2$ , 16.51, df=12, p=0.169), but associated with the occurrence of chronic pain ( $\chi^2$ , 34.39, df=4, p<0.001) as well as with the frequency of pain ( $\chi^2$ , 25.62, df=8, p=0.001).

Chronic pain was also associated with higher levels of stress at work, even if the mean difference was small (6.61 vs 5.47, SD=2.39/2.49, p<0.001).

Intraoperative findings of spread of endometriosis lesions showed varying associations with health-related limitations in career choice: having endometriosis lesions at the pelvic wall ( $\chi^2$ , 11.14, df=4, p=0.025) or in the sacrouterine ligaments ( $\chi^2$ , 13.51, df=4, p=0.009) was significantly associated with greater limitations in career choice, while such an outcome could not be found for localization in the vaginal fornix, for an obliteration of Douglas, or for adhesions. Higher levels of stress

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3 378 at work were associated with intra-abdominal adhesions (mean 6.36 vs 5.50,  
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5 379 SD=2.46/2.48, p=0.001), but not with other intraoperative findings.  
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### 8 9 381 **Work impairment and compensatory mechanisms**

10  
11 382 Asked about the amount of sick leave due to endometriosis during the last month,  
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13 383 78.1% of the women of the case group reported no sick leave, 8.5% reported one to  
14  
15 384 three days, 3.1% reported four to seven days, 2.0% reported one to two weeks and  
16  
17 385 8.1% reported two to four weeks.

18  
19 386 Altogether, 13.1% of endometriosis patients used one week or more of overtime or  
20  
21 387 vacation during the last year when they felt too sick to work due to symptoms of  
22  
23 388 endometriosis. Furthermore, 75.5% of women with endometriosis reported to have  
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25 389 gone to work during the previous month in spite of severe pain. Asked about the  
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27 390 previous year, 89.2% of women with endometriosis affirmed to have worked despite  
28  
29 391 pain. Out of the women diagnosed with endometriosis, 89.8% noted a loss of work  
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31 392 productivity due to endometriosis, with 65.1% reporting strong or very strong  
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33 393 limitations when symptoms were severe. On days with minimal endometriosis  
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35 394 symptoms, 75.3% still felt some degree of loss of productivity.

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37 395 A minority of women with endometriosis reported working part time (10.3%) or giving  
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39 396 up work entirely (5.8%) due to their disease (n=445).  
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### 45 46 398 **Association of endometriosis-related symptoms with sick leave and** 47 48 399 **productivity loss**

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50 400 We then examined whether different endometriosis symptoms were related to  
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52 401 absenteeism and impaired work productivity (Table IV).  
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403 **Table IV: Association of endometriosis-related symptoms to sick leave and**  
 404 **productivity loss in the last month**  
 405

Predictor		Sick leave <sup>a</sup>		Productivity loss <sup>b</sup>	
		OR (95% CI)	R <sup>2</sup>	OR (95% CI)	R <sup>2</sup>
Chronic pain	Yes	3.52 (2.02; 6.13); p<0.001 <sup>#</sup>	0.072	3.08 (2.11; 4.50); p<0.001 <sup>#</sup>	0.087
	No	Ref.		Ref.	
Frequency of pain	Daily	2.82 (1.47; 5.39); p=0.002 <sup>#</sup>	0.053	1.81 (1.05; 3.12); p=0.032	0.040
	>1 per week ≤1 per week	1.40 (0.66; 2.97); p=0.377 Ref.		0.76 (0.42; 1.38); p=0.369 Ref.	
Frequency of fatigue	Frequently	3.50 (1.76; 6.94); p<0.001 <sup>#</sup>	0.073	3.99 (2.49; 6.39); p<0.001 <sup>#</sup>	0.107
	Sometimes Rarely	1.15 (0.50; 2.64); p=0.748 Ref.		1.44 (0.86; 2.41); p=0.168 Ref.	
Psychological symptoms <sup>c</sup>	Yes	3.03 (1.77; 5.18); p<0.001 <sup>#</sup>	0.061	2.90 (1.98; 4.23); p<0.001 <sup>#</sup>	0.082
	No	Ref.		Ref.	

406 *Note*

407 <sup>#</sup> Statistically significant at Bonferroni corrected  $\alpha=0.01$

408 <sup>a</sup> Refers to the last 4 weeks; Scale: 1="never", 2=1-7 days, 3=>7 days

409 <sup>b</sup> Refers to current maximal impairments; Scale: 1="not at all/little", 2="moderately/strong", 3="very strong"

410 <sup>c</sup> depressive mood/anxiety/reduced resilience of more than three months

411  
 412 Corrected for multiple testing, all four predictor variables were significantly associated  
 413 with sick leave during the previous four weeks. The occurrence of chronic pain as  
 414 well as the frequency of fatigue and concomitant psychological symptoms were  
 415 associated with significantly higher degrees of perceived productivity loss. Including  
 416 age and time since diagnosis as potential confounders did not alter the results.  
 417 Likewise, the factor of different localisations of endometriosis was not associated with  
 418 sick leave or productivity loss (all p>0.05).

## 421 Discussion

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 423 Endometriosis is associated with impairment of professional activity: women  
 424 diagnosed with endometriosis showed a lower likelihood of working in their desired

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3 425 profession and stronger health-related limitations in their career decisions. In  
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5 426 contrast, they had professional experience of longer durations. All of these main  
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7 427 outcomes were not reported previously and open new insights into the professional  
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9 428 life of women with endometriosis. Endometriosis-associated symptoms and symptom  
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11 429 characteristics were moderately related to sick leave and loss of productivity, but in  
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13 430 contrast to our expectations, endometriosis was not associated with increased work-  
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15 431 related stress levels.  
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20 433 In contrast to remarkable differences regarding parameters of working life, education  
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22 434 level did not differ significantly between case and control groups (Table I); this is a  
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24 435 result that has been described previously.<sup>17</sup> Other studies, however, reported serious  
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26 436 effects of endometriosis on education level, especially on tertiary formation.<sup>12 24</sup>  
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28 437 These contrasting findings might result from differences in study groups, e.g. with  
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30 438 regard to the onset of disease symptoms in relation to education, professional  
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32 439 training and professional activity. Many studies report an average age of first  
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34 440 symptoms between 20 and 29 years,<sup>10 38-40</sup>. In our study the average age of  
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36 441 diagnosis is 33.7 years. Even if many of these women report the onset of  
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38 442 endometriosis-related symptoms several years before diagnosis, it is still an age at  
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40 443 which most women have completed professional training. As a consequence, the  
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42 444 women investigated in such cohorts will not experience a negative impact of  
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44 445 endometriosis on their education, because they were still symptom-free at this age.  
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46 446 Other authors reported an earlier onset of disease symptoms,<sup>41</sup> and emphasized that  
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48 447 endometriosis in adolescent girls was an underestimated problem.<sup>40 42 43</sup>  
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50 448 Consequently, those women, which suffer from endometriosis symptoms already at a  
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52 449 young age, might feel limitations due to the disease also early in life, namely already  
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54 450 during education.  
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3 451 On the other hand, there might be a higher tolerance for sick leave and impaired  
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5 452 energy levels in a school or university setting compared to in paid employment.  
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9 454 Health issues are important criteria in career choice, and women diagnosed with  
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11 455 endometriosis do work less often in their desired profession. However, women with  
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13 456 endometriosis reported a greater length of experience in the current profession  
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15 457 (Table IIIb). Professional experience and the length of time a woman is working with  
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17 458 the current employer are highly correlated. These results can be interpreted  
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19 459 positively in the sense that women with endometriosis were successful in carefully  
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21 460 choosing a long-term profession. On the other hand, women might feel less able to  
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23 461 change the professional field and stuck in an undesired profession because of  
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25 462 endometriosis.  
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31 464 Several authors reported elevated levels of general<sup>44 45</sup> as well as emotional<sup>21</sup>  
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33 465 distress in women diagnosed with endometriosis. This first study on work-specific  
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35 466 stress in endometriosis affected women produced results in contrast to our  
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37 467 expectations. Even though women reported that they sometimes went to work  
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39 468 despite endometriosis-associated pain, women with endometriosis did not  
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41 469 experience higher work-related stress levels than the control women; but within the  
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43 470 group of women with endometriosis, those with chronic pain reported significantly  
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45 471 higher work-related stress than those without pain. We investigated women whose  
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47 472 initial diagnosis was up to 20 years ago; these women may have meanwhile found an  
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49 473 occupation meeting their needs, and superiors and colleagues may have adapted to  
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51 474 their sometimes reduced availability for work. Also, the fact that work can be a source  
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53 475 of distraction and of self-esteem for individuals suffering from a chronic disease<sup>46</sup>  
54  
55 476 may offset stressful situations.  
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3 477 According to our results and those of others,<sup>41</sup> women affected by endometriosis  
4 478 compensate for their health-related restrictions at work by using overtime or vacation  
5 479 for absences as well as by saving energy for work through reduction of leisure time  
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7 480 activities.  
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13 482 Despite these personal efforts to adapt to an adverse situation, productivity loss<sup>9 15</sup>  
14 483 and sick leave<sup>9 10</sup> are relevant issues for many women diagnosed with endometriosis.  
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16 484 Average loss of work time per week (absenteeism) due to endometriosis is reported  
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18 485 to be between 4.4 and 7.4 hours.<sup>13 14</sup> In our study, chronic pain, the frequency of  
19  
20 486 pain, fatigue, and psychological symptoms, such as self-reported depression and  
21  
22 487 anxiety, were significantly - but with modest effect sizes - related to taking more sick  
23  
24 488 leave (Table IV). Productivity loss at work due to endometriosis-related symptoms  
25  
26 489 was described to be high or very high – depending on the current severity of  
27  
28 490 symptoms – by up to 65% of women in the present study. Struggles to fulfil normal  
29  
30 491 demands of work might be exacerbated by the side effects of treatment, for example  
31  
32 492 by dizziness from strong pain killers.<sup>22 23</sup> Although, the majority of women affected  
33  
34 493 with endometriosis seemed to be able to compensate for disease-related difficulties  
35  
36 494 at work and to realize successful long-term professional activity, 16.2% of the women  
37  
38 495 nevertheless reduced or even gave up work entirely due to endometriosis-related  
39  
40 496 symptoms; this is a situation that has been observed also by others.<sup>17</sup> Furthermore, a  
41  
42 497 very similar percentage of women with endometriosis and control women worked part  
43  
44 498 time, even though women diagnosed with endometriosis remained childless more  
45  
46 499 often. Such decisions may result from feeling pressured to reduce or quit work when  
47  
48 500 employers know about a chronic disease such as endometriosis.<sup>12 24</sup> More flexible  
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50 501 work schedules, a generous policy regarding sick leave, sufficient breaks, adjusted  
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52 502 physical demands, the possibility to lie down, and the existence of bathrooms nearby  
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3 503 are seen to be helpful resources for successful professional performance in women  
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5 504 with endometriosis.<sup>23 24</sup>  
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9 506 As for the relationship between rASRM stage and endometriosis-associated  
10  
11 507 symptoms,<sup>1 3</sup> none of the parameters evaluating professional activity showed any  
12  
13 508 significant association with rARSM stage. Testing the association between different  
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15 509 intraoperative findings of endometriotic lesions and work outcomes showed  
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17 510 inconsistent results. In contrast, most outcome measures were related to the  
18  
19 511 occurrence and frequency of chronic pain; this result is supported by other studies on  
20  
21 512 endometriosis,<sup>14 19</sup> as well as on other chronic pain conditions such as migraine or  
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23 513 fibromyalgia.<sup>47 48</sup> Even if the effect size of pain on work in this study is limited,  
24  
25 514 findings support the relevance of pain management for satisfactory work  
26  
27 515 performance. Fatigue, either as a symptom of endometriosis or as a frequent  
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29 516 comorbidity,<sup>49</sup> interfered with professional activity in this as well as in other studies.<sup>1</sup>  
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31 517 <sup>13</sup>

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35 518 In summary, it may be that women with endometriosis strive for normality at their  
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37 519 work place, even if it is associated with reduced professional flexibility or with giving  
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39 520 up the desire for another profession.  
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44 522 This study presents one of the largest samples investigating the association between  
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46 523 endometriosis and professional life and it is one of the very few studies providing a  
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48 524 control group. Study participants were recruited in university hospitals, in district  
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50 525 hospitals and in doctors' practices in order to collect a representative sample. The  
51  
52 526 pair matching with regard to age and ethnic background reduced the confounding  
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54 527 effect of these factors. A meticulous review of all surgical records by the same  
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56 528 investigator (AKS) ensured high data quality with regard to diagnosis and  
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3 529 classification of endometriosis. The response rate of 64.1% in the case group is in  
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5 530 the upper level of comparable studies,<sup>12 13</sup> whereas the response rate of 35.8% in the  
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7 531 control group is comparatively low. We cannot exclude that women with a particularly  
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9 532 high work load refrained from study participation; however, such an effect is equally  
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11 533 relevant in women diagnosed with endometriosis and in controls. The higher  
12  
13 534 response rate in women with endometriosis supports the fact that such an  
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15 535 association does not represent a particular problem for members in this group.  
16  
17 536 Given the methodology of a self-reported questionnaire answered retrospectively,  
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19 537 distortions in the sense of falsely or overly attributing dissatisfaction on the job to  
20  
21 538 endometriosis cannot be excluded. By addressing questions on professional activity  
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23 539 either current or in the period just prior to study participation, we tried to reduce recall  
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25 540 bias. As we included only patients with a confirmed diagnosis of endometriosis, and  
26  
27 541 as such a confirmation can be provided only by surgery, there may be referral bias.  
28  
29 542 For example, affected but asymptomatic women and symptomatic women who do  
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31 543 not have access to or refused surgery might have been excluded, with the first false  
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33 544 categorization might result in over- and the second in underestimation of the results.  
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35 545 In contrast, asymptomatic women with endometriosis might have been included in  
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37 546 the control group which would result in underestimation of results. As we have no  
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39 547 differentiated information on symptoms resulting from diseases other than  
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41 548 endometriosis, in both groups further confounders might be present; this would also  
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43 549 result in underestimation of our findings. Although we recruited women diagnosed  
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45 550 with endometriosis independent from their acute symptomatology e.g. also those  
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47 551 presenting for regular controls, recruitment through hospitals might have resulted in  
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49 552 selection of women with more severe disease symptoms. A comparison group for the  
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51 553 questions of sick leave and productivity loss at work would have been beneficial.  
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53 554 However, analysis of impact of different endometriosis-related symptoms on these  
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3 555 two outcomes allowed for indirect conclusions on the association between  
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5 556 endometriosis and reduced working ability, as well as basic data to design future  
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7 557 studies.  
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## 12 13 560 **Conclusion**

14  
15 561 Even if most measured effect sizes of associations between endometriosis and  
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17 562 individual parameters of working life were small, the study indicates a burdensome  
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19 563 influence of the disease on the working life of women affected by endometriosis.  
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21 564 Therefore, medical and psychological support should be sensitised towards such  
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23 565 issues in order to support women in managing their working life and adjusting their  
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25 566 professional choices and professional development to individual endometriosis-  
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27 567 related conditions if needed. Furthermore, for professionals in occupational medicine,  
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29 568 insurances, politics etc. it might be useful to know about endometriosis-related  
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31 569 challenges and possible limitations in professional activity.  
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51  
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54 579 manuscript.  
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7 583 **Authors roles**

8  
9 584 MLS: collection of data on site in Solothurn and Schaffhausen, interpretation of data,  
10  
11 585 drafting and finalization of the manuscript

12  
13 586 MPH: statistical analysis, interpretation of data, finalization of manuscript

14  
15 587 AKS: investigator, collection of data on site in Winterthur, Switzerland, verification of  
16  
17 588 surgical reports, finalization of the manuscript

18  
19 589 KG: concept of study, collection of data on site in Zurich, management databank,  
20  
21 590 finalization of the manuscript

22  
23 591 MR: investigator, collection of data on site in Berlin, Germany, finalization of the  
24  
25 592 manuscript

26  
27 593 MW: investigator, collection of data on site in Aachen, Germany, and in Graz,  
28  
29 594 Austria, finalization of the manuscript

30  
31 595 FH: investigator, collection of data on site in St. Gallen, Switzerland, finalization of  
32  
33 596 the manuscript

34  
35 597 SvO: investigator, collection of data on site in Zurich, Switzerland, finalization of the  
36  
37 598 manuscript

38  
39 599 ME: investigator, collection of data on site in Schaffhausen, Switzerland, finalization  
40  
41 600 of the manuscript

42  
43 601 FM: concept of study, investigator on site in Solothurn, Switzerland, finalization of  
44  
45 602 manuscript

46  
47 603 BI: concept of study, investigator on site in Zurich, Switzerland, interpretation of data,  
48  
49 604 finalization of manuscript

50  
51 605 PI: concept of study, investigator and data collection in Zurich, Switzerland,  
52  
53 606 finalization of the manuscript

1  
2  
3 607 BL: principal investigator, concept and conduct of study, investigator on site in Zurich,  
4  
5 608 Switzerland, collection and analysis of data, preparation and finalization of  
6  
7 609 manuscript  
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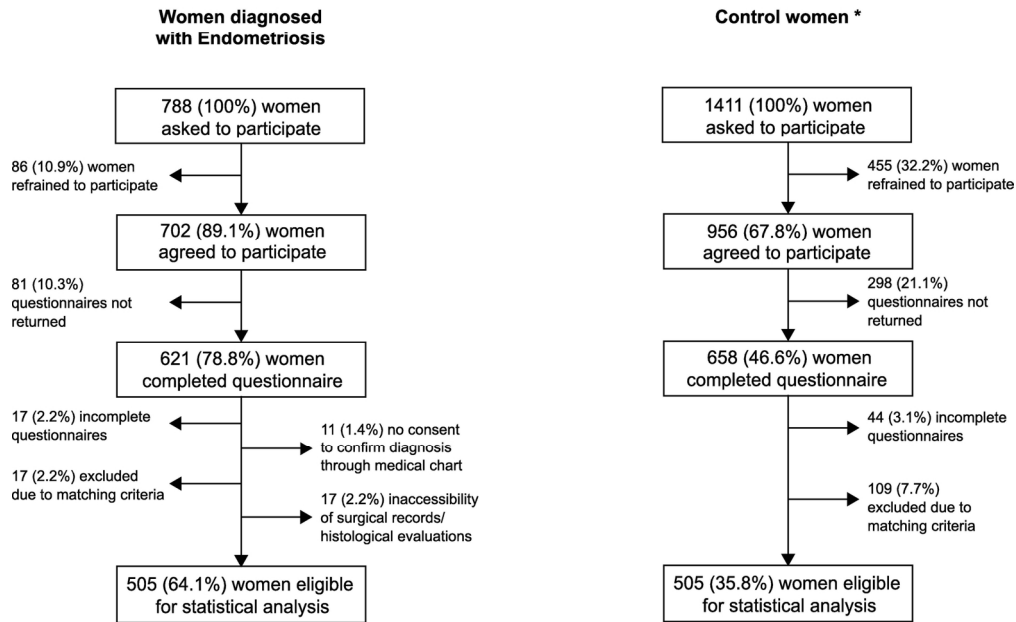
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18 740 **Figure Legend**

19  
20 741 Fig 1.: Recruitment of study participants  
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Figure I. Recruitment of study participants



\* women presenting for routine gynaecological care or benign gynaecological surgery

157x130mm (300 x 300 DPI)

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4/5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8/9
Bias	9	Describe any efforts to address potential sources of bias	8/9
Study size	10	Explain how the study size was arrived at	6/7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	7

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N in tables
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Tables, 11-16
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables, 11-16
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Tables, 11-16
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).